

09/938,235

FULL ESTIMATED COST

ENTRY	SESSION
0.21	0.21

FILE 'REGISTRY' ENTERED AT 16:23:16 ON 26 OCT 2004
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Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES: 25 OCT 2004 HIGHEST RN 769101-30-6
DICTIONARY FILE UPDATES: 25 OCT 2004 HIGHEST RN 769101-30-6

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
<http://www.cas.org/ONLINE/DBSS/registryss.html>

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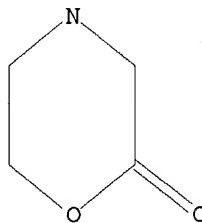
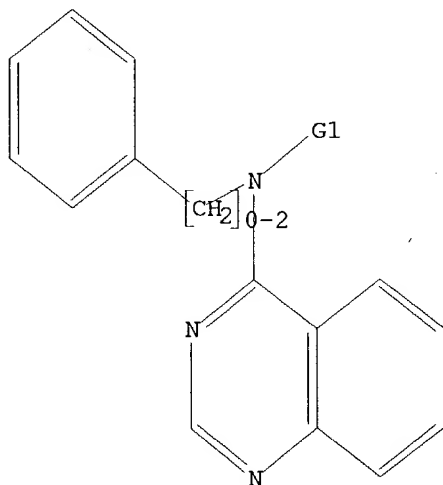
Uploading C:\Program Files\Stnexp\Queries\938235.str

L1 STRUCTURE UPLOADED

=> d l1

L1 HAS NO ANSWERS

L1 STR



G1 H, Me, Et, n-Pr, i-Pr, n-Bu, i-Bu, s-Bu, t-Bu

Structure attributes must be viewed using STN Express query preparation.

=> s l1 sss full

09/938,235

FULL SEARCH INITIATED 16:23:46 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 142 TO ITERATE

100.0% PROCESSED 142 ITERATIONS 119 ANSWERS
SEARCH TIME: 00.00.01

L2 119 SEA SSS FUL L1

=> file caplus

COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
155.42	155.63

FULL ESTIMATED COST

FILE 'CAPLUS' ENTERED AT 16:23:53 ON 26 OCT 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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FILE COVERS 1907 - 26 Oct 2004 VOL 141 ISS 18
FILE LAST UPDATED: 25 Oct 2004 (20041025/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s 12

L3 13 L2

=> d 13 1-13 ibib abs hitstr

L3 ANSWER 1 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2004:60252 CAPLUS

DOCUMENT NUMBER: 140:128427

TITLE: Preparation of quinazolines as ephrin and EGFR receptor kinase modulators for treating cancer and other disorders

INVENTOR(S): Rice, Kenneth D.; Anand, Neel Kumar; Bussenius, Joerg; Costanzo, Simona; Kennedy, Abigail R.; Kim, Angie I.; Peto, Csaba J.; Tsang, Tsze H.; Blazey, Charles M.

PATENT ASSIGNEE(S): Exelixis, Inc., USA

SOURCE: PCT Int. Appl., 266 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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Date not good

WO 2004006846 A2 20040122 WO 2003-US21923 20030714
 WO 2004006846 A3 20040715
 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
 CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
 GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
 LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
 PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,
 TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY,
 KG, KZ, MD, RU
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
 CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC,
 NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ,
 GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:

US 2002-396269P P 20020715
 US 2003-447212P P 20030213

OTHER SOURCE(S): MARPAT 140:128427

GI

no non provisionals
 yet

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The present invention provides quinazolines (shown as I; variables defined below; e.g. II and III) for modulating receptor tyrosine kinase activity, particularly ephrin and EGFR, and methods of treating diseases mediated by receptor kinase activity using the compds. and pharmaceutical compns. thereof. Diseases mediated by receptor kinase activity include, but are not limited to, diseases characterized in part by abnormal levels of cell proliferation (i.e. tumor growth), programmed cell death (apoptosis), cell migration and invasion and angiogenesis associated with tumor growth. Compds. of the invention include 'spectrum selective' kinase modulators, compds. that inhibit, regulate and/or modulate signal transduction across subfamilies of receptor-type tyrosine kinases, including ephrin and EGFR. Inhibitory activities for >200 examples of I are tabulated for some or all of EphB4, EphA2, KDR, Flt-1, EGFR and ErbB2 kinases. Although the methods of preparation are not claimed, 37 example preps. are included. For example, 1,4:3,6-dianhydro-2-O-[4-[(3-chloro-2-methylphenyl)amino]-6-(methyloxy)quinazolin-7-yl]-5-O-methyl-L-iditol hydrochloride was prepared in 2 steps (94, 51 % yields, resp.) starting with mesylation of 1,4:3,6-dianhydro-2-O-methyl-D-glucitol followed by ether formation of the intermediate 1,4:3,6-dianhydro-2-O-methyl-5-O-(methylsulfonyl)-D-glucitol with 4-[(3,4-dichlorophenyl)amino]-6-(methyloxy)quinazolin-7-ol; the quinazolinol was prepared in 64 % yield from 4-chloro-6-(methyloxy)-7-[(phenylmethyl)oxy]quinazoline hydrochloride and 3,4-dichloroaniline. For I: R1 is C1-C3 (un)substituted alkyl; R2 = H, halogen, trihalomethyl, CN, NH2, NO2, OR3, N(R3)R4, S(O)O-2R4, SO2N(R3)R4, CO2R3, C(O)N(R3)R4, N(R3)SO2R4, N(R3)C(O)R3, N(R3)CO2R4, C(O)R3, (un)substituted lower alkyl, (un)substituted lower alkenyl, and (un)substituted lower alkynyl; R3 is H or R4; R4 = (un)substituted lower alkyl, (un)substituted aryl, (un)substituted lower arylalkyl, (un)substituted heterocyclyl, and (un)substituted lower heterocyclylalkyl; or R3 and R4, when taken together with a common N to which they are attached, form an (un)substituted 5-7-membered heterocyclyl, said (un)substituted five-to seven-membered heterocyclyl optionally containing at least one addnl. heteroatom = N, O, S, and P. Q is 0-5; Z = OCH2, O, S(O)O-2, N(R5)CH2, and NR5; R5 is -H or (un)substituted lower alkyl; M1 is H, (un)substituted C1-C8 alkyl-L2-L1, G(CH2)O-3, or R53(R54)N(CH2)O-3; wherein G is a saturated 5-7-membered heterocyclyl containing 1-2 annular heteroatoms; L1 is C:O or SO2; L2 is a direct bond, O, or NH; M2 is a saturated or mono- or polyunsatd. C3-C14 mono-

or fused-polycyclic hydrocarbonyl optionally containing 1-3 annular heteroatoms per ring; M3 is NR9, O, or absent; M4 is CH2, CH2CH2, CH2CH2CH2, or absent; addnl. details are given in the claims.

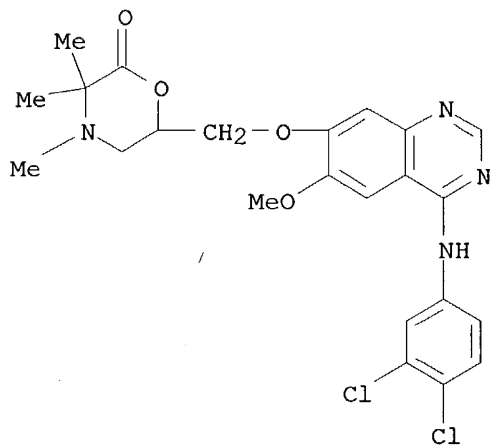
IT **650582-58-4P**

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug candidate; preparation of quinazolines as ephrin and EGFR receptor kinase modulators for treating cancer and other disorders)

RN 650582-58-4 CAPLUS

CN 2-Morpholinone, 6-[[[4-[(3,4-dichlorophenyl)amino]-6-methoxy-7-quinazolinyl]oxy]methyl]-3,3,4-trimethyl- (9CI) (CA INDEX NAME)



L3 ANSWER 2 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2004:41317 CAPLUS

DOCUMENT NUMBER: 140:99649

TITLE: Pharmaceutical compositions for the treatment of respiratory tract diseases comprising novel anticholinergic agents and inhibitors of EGFR-kinase

INVENTOR(S): Pairet, Michel; Meade, Christopher John Montague; Pieper, Michael P.

PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma GmbH & Co. Kg, Germany

SOURCE: PCT Int. Appl., 44 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

assigned complex compositions

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004004775	A1	20040115	WO 2003-EP6788	20030626
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,			

09/938,235

CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC,
NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ,
GW, ML, MR, NE, SN, TD, TG

DE 10230751 A1 20040122 DE 2002-10230751 20020709
US 2004048887 A1 20040311 US 2003-614382 20030707

PRIORITY APPLN. INFO.: DE 2002-10230751 A 20020709
US 2002-407746P P 20020903

OTHER SOURCE(S): MARPAT 140:99649

AB The invention relates to novel pharmaceutical compns. comprising novel anticholinergic agents and EGFR-kinase inhibitors, method for production and use thereof in the treatment of respiratory diseases. The synthesis of several EGFR-kinase inhibitors is given. Thus an inhalation capsule contained (microgram/capsule): 2,2-Diphenylpropionic acid scopine ester methobromide 60; EGFR kinase inhibitor 3500; lactose.3440.

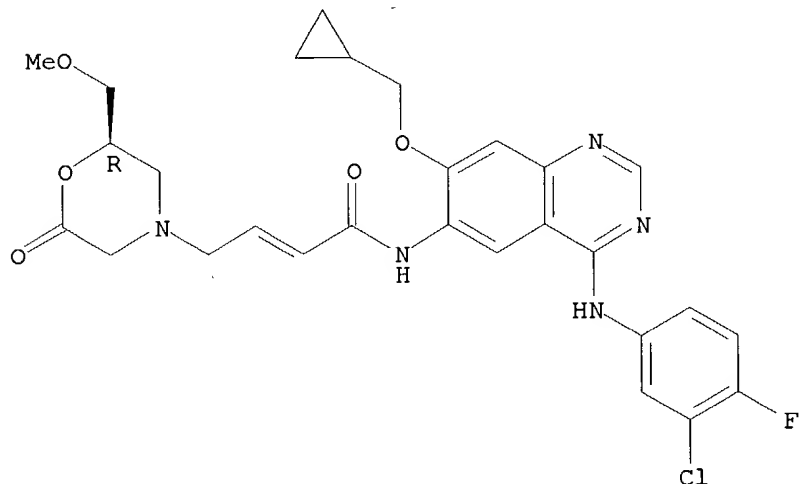
IT 402569-98-6P 402724-01-0P 402724-11-2P
402724-17-8P 402724-18-9P 402734-65-0P
402735-03-9P 402855-52-1P 402855-53-2P
402855-58-7P

RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use);
BIOL (Biological study); PREP (Preparation); USES (Uses)
(pharmaceutical compns. for treatment of respiratory tract diseases
comprising anticholinergic agents and inhibitors of EGFR-kinase)

RN 402569-98-6 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-
6-quinazolinyl]-4-[(2R)-2-(methoxymethyl)-6-oxo-4-morpholinyl]- (9CI) (CA
INDEX NAME)

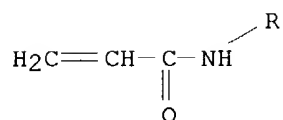
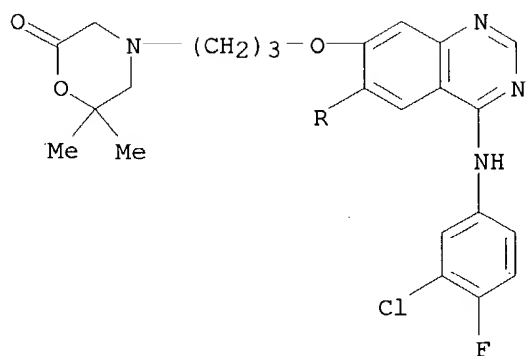
Absolute stereochemistry.
Double bond geometry unknown.



RN 402724-01-0 CAPLUS

CN 2-Propenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[3-(2,2-dimethyl-6-
oxo-4-morpholinyl)propoxy]-6-quinazolinyl]- (9CI) (CA INDEX NAME)

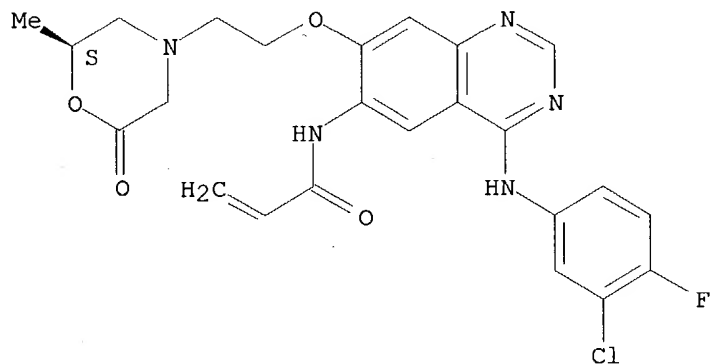
09/938,235



RN 402724-11-2 CAPLUS

CN 2-Propenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[2-[(2S)-2-methyl-6-oxo-4-morpholinyl]ethoxy]-6-quinazolinyl]- (9CI) (CA INDEX NAME)

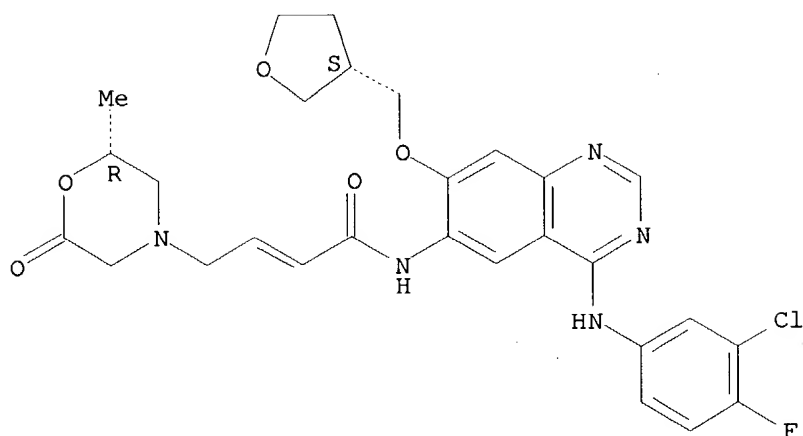
Absolute stereochemistry.



RN 402724-17-8 CAPLUS

CN 2-Propenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[4-[(2R)-2-methyl-6-oxo-4-morpholinyl]butoxy]-6-quinazolinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 3 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:656610 CAPLUS

DOCUMENT NUMBER: 139:202486

TITLE: Inhalants containing anticholinergic agents and EGFR kinase inhibitors

INVENTOR(S): Jung, Birgit; Pairet, Michel; Pieper, Michael P.

PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma G.m.b.H. & Co. K.-G., Germany

SOURCE: PCT Int. Appl., 50 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

assigned complex composition

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003068264	A1	20030821	WO 2003-EP1357	20030212
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10206505	A1	20030828	DE 2002-10206505	20020216
US 2003158196	A1	20030821	US 2003-360064	20030207
PRIORITY APPLN. INFO.:				
			DE 2002-10206505	A 20020216
			US 2002-369213P	P 20020401

AB The invention relates to novel medicinal compns. on the basis of anticholinergic agents and EGFR kinase inhibitors, methods for their production and their use for treating respiratory diseases. Thus a series of quinazoline derivs. were synthesized that were EGFR kinase inhibitors. A typical inhalation powder contained (μ g/capsule): tiotropium bromide 10.8; EGFR kinase inhibitor 3500; lactose 3489.2.

IT 402569-98-6P 402724-01-0P 402724-05-4P

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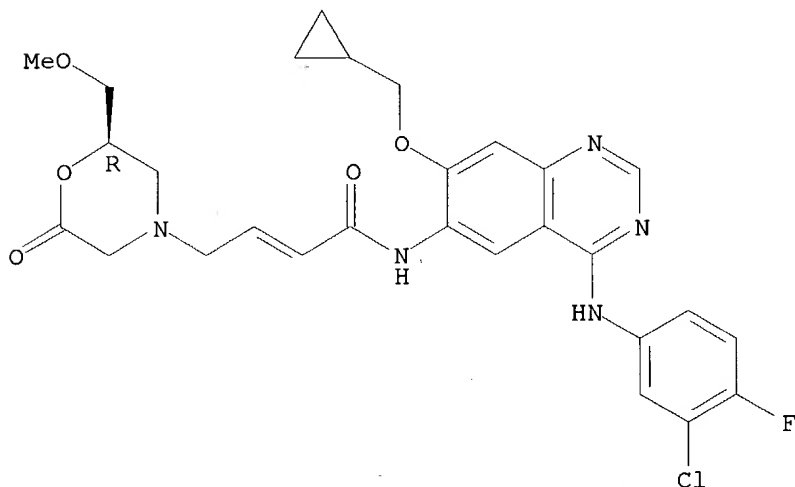
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402735-03-9P 402855-52-1P 402855-53-2P
402855-58-7P

RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use);
BIOL (Biological study); PREP (Preparation); USES (Uses)
(inhalants containing anticholinergic agents and EGFR kinase inhibitors)

RN 402569-98-6 CAPLUS

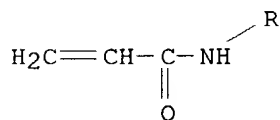
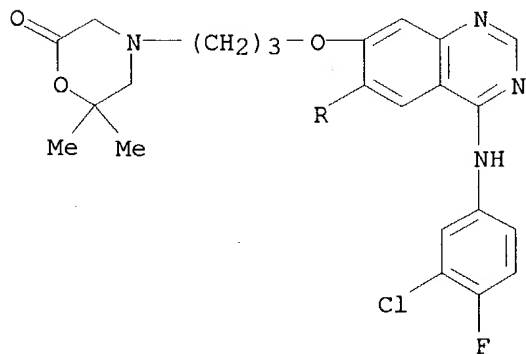
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-
6-quinazolinyl]-4-[(2R)-2-(methoxymethyl)-6-oxo-4-morpholinyl]- (9CI) (CA
INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



RN 402724-01-0 CAPLUS

CN 2-Propenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[3-(2,2-dimethyl-6-
oxo-4-morpholinyl)propoxy]-6-quinazolinyl]- (9CI) (CA INDEX NAME)



RN 402724-05-4 CAPLUS

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 4 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:607455 CAPLUS

DOCUMENT NUMBER: 139:159940

TITLE: Use of tyrosine kinase inhibitors for treatment of pulmonary inflammatory conditions

INVENTOR(S): Jung, Birgit; Puschner, Hubert

PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma G.m.b.H. & Co. K.-G., Germany

SOURCE: Ger. Offen., 24 pp.

CODEN: GWXXBX

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

assigned

different substitution

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10204462	A1	20030807	DE 2002-10204462	20020205
WO 2003066060	A2	20030814	WO 2003-EP814	20030128
WO 2003066060	A3	20040115		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2003149062 A1 20030807 US 2003-353616 20030129
 PRIORITY APPLN. INFO.: DE 2002-10204462 A 20020205

OTHER SOURCE(S): MARPAT 139:159940

AB The invention discloses the use of quinazoline derivs. (Markush included), or the compds. (1) 4-[(3-chloro-4-fluorophenyl)amino]-6-[(4-dimethylaminocyclohexyl)amino]pyrimido[5,4-d]pyrimidine; (2) 4-[(R)-(1-phenylethyl)amino]-6-(4-hydroxyphenyl)-7H-pyrrolo[2,3-d]pyrimidine; (3) 4-[(3-Chloro-4-(3-fluoro-4-benzyloxy)phenyl)amino]-6-[5-((2-methansulfonyl)ethyl)amino)methyl]-furan-2-yl]quinazoline; or the antibody cetuximab C225, trastuzumab, ABX-EGF, Mab ICR-62 and EGFR antisense, their tautomers, their stereoisomers and their salts, in particular their physiol. compatible salts with inorg. or organic acids or bases, for the production of a medication for prevention or treatment of diseases of the respiratory system or the lung. Preparation of quinazoline compds. is included.

IT 402724-01-0P 402724-11-2P 402724-18-9P
 402724-19-0P 402734-65-0P 402735-03-9P
 402855-52-1P 402855-58-7P

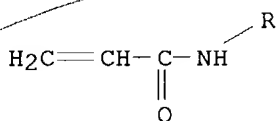
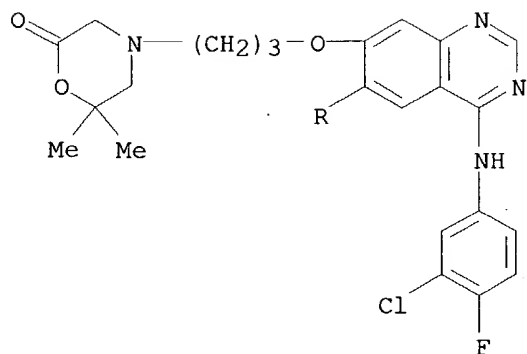
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(tyrosine kinase inhibitors for treatment of pulmonary inflammatory conditions)

RN 402724-01-0 CAPLUS

CN 2-Propenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[3-(2,2-dimethyl-6-oxo-4-morpholinyl)propoxy]-6-quinazolinyl]- (9CI) (CA INDEX NAME)

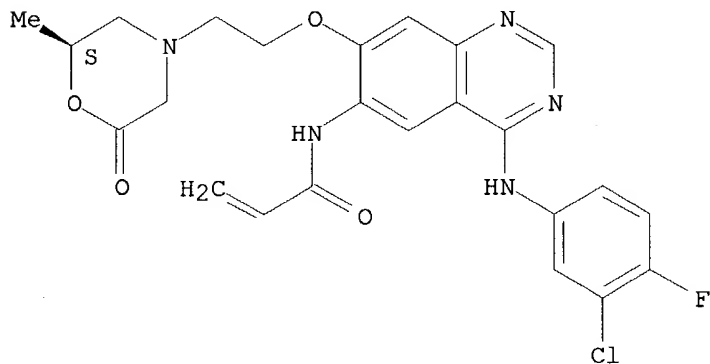
09/938,235



RN 402724-11-2 CAPLUS

CN 2-Propenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[2-[(2S)-2-methyl-6-oxo-4-morpholinyl]ethoxy]-6-quinazolinyl]- (9CI) (CA INDEX NAME)

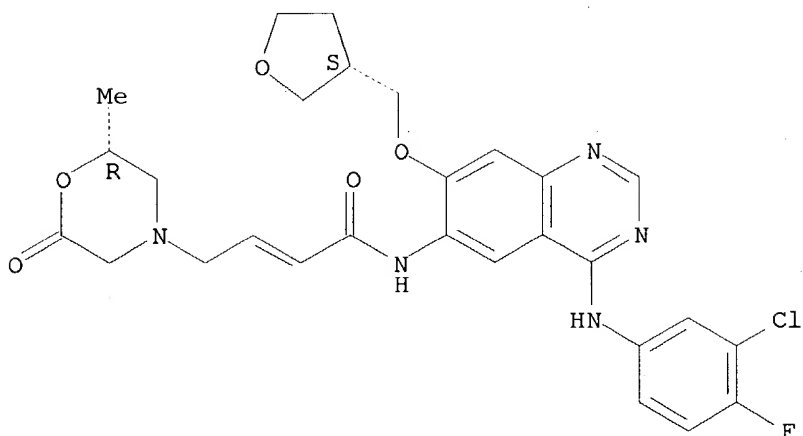
Absolute stereochemistry.



RN 402724-18-9 CAPLUS

CN 2-Propenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[4-[(2S)-2-methyl-6-oxo-4-morpholinyl]butoxy]-6-quinazolinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

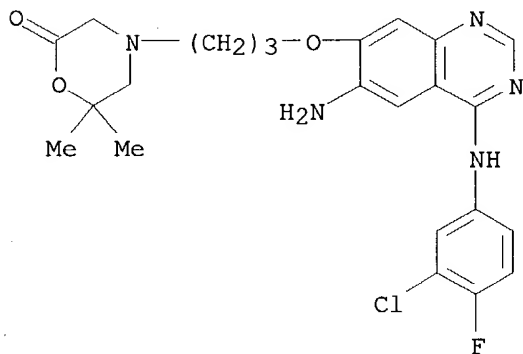


IT 402723-54-0

RL: RCT (Reactant); RACT (Reactant or reagent)
(tyrosine kinase inhibitors for treatment of pulmonary inflammatory conditions)

RN 402723-54-0 CAPLUS

CN 2-Morpholinone, 4-[3-[[6-amino-4-[(3-chloro-4-fluorophenyl)amino]-7-quinazolinyl]oxy]propyl]-6,6-dimethyl- (9CI) (CA INDEX NAME)



L3 ANSWER 5 OF 13 CARLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:171892 CAPLUS

DOCUMENT NUMBER: 136:216762

TITLE: Preparation of 4-amino-6-heterocyclylcarbonylaminoquinazolines as epidermal growth factor receptor signal transduction inhibitors

INVENTOR(S): Himmelsbach, Frank; Langkopf, Elke; Jung, Birgit; Blech, Stefan; Solca, Flavio

PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma Kg, Germany

SOURCE: PCT Int. Appl., 53 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

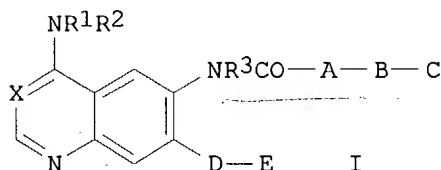
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

diff sub *assigned*
6,740,691

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2002018376 A1 20020307 WO 2001-EP9536 20010818
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL,
PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG,
US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
DE 10042062 A1 20020307 DE 2000-10042062 20000826
AU 2001095482 A5 20020313 AU 2001-95482 20010818
EP 1315720 A1 20030604 EP 2001-976108 20010818
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
JP 2004507538 T2 20040311 JP 2002-523891 20010818
US 2002115675 A1 20020822 US 2001-934631 20010822
US 6740651 B2 20040525
PRIORITY APPLN. INFO.: DE 2000-10042062 A 20000826
US 2000-230542P P 20000905
WO 2001-EP9536 W 20010818
OTHER SOURCE(S): MARPAT 136:216762
GI



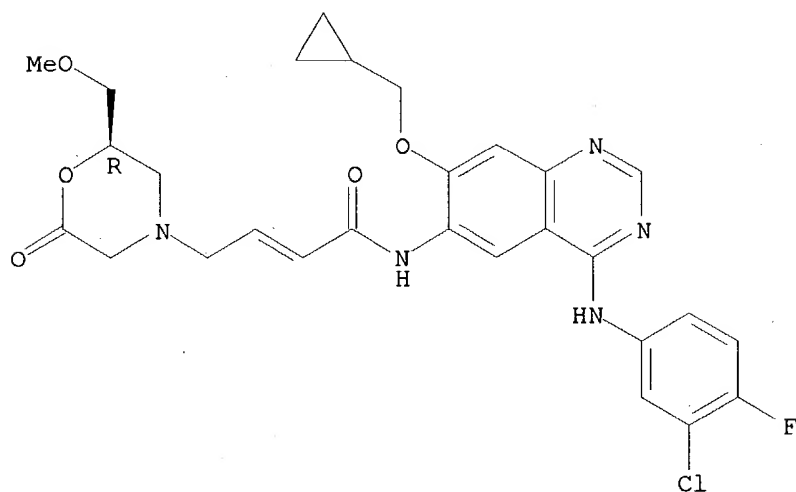
AB Title compds. [I; X = N, (substituted) methynyl; R₁ = H, Me; R₂ = (substituted) Ph, PhCH₂, 1-phenylethyl; R₃ = H, Me; A = (substituted) vinyl, ethynyl, 1,3-butadien-1,4-yl; B = (substituted) alkenyl, alkenylcarbonyl, etc.; C = (substituted) 2-oxomorpholin-4-yl, etc; D = oxyalkenyl, O; E = (substituted) amino, alkenylimino, imidazolyl, cycloalkyl; or DE = H, (substituted) alkoxy, etc.], were prepared Thus, 4-[(3-chloro-4-fluorophenyl)amino]-6-[(4-[N-(ethoxycarbonylmethyl)-N-((R)-2-hydroxy-3-methoxypropyl)amino]-1-oxo-2-buten-1-yl)amino]-7-cyclopropylmethoxyquinazoline (preparation given) and MeSO₂OH in MeCN were stirred for 4 h under reflux to give 69% 4-[(3-chloro-4-fluorophenyl)amino]-6-[(4-[(R)-2-methoxymethyl-6-oxomorpholin-4-yl]-1-oxo-2-buten-1-yl)amino]-7-cyclopropylmethoxyquinazoline. The latter inhibited epidermal growth factor (EGF)-dependent proliferation of F/L-HERc cells with IC₅₀ = 2 nM. The invention relates to the use of the title compds. for treating tumor diseases, and lung and respiratory tract disorders.

IT **402569-98-6P 402570-00-7P 402570-01-8P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of (amino)(heterocyclylcarbonylamino)quinazolines as epidermal growth factor receptor signal transduction inhibitors)

RN 402569-98-6 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[(2R)-2-(methoxymethyl)-6-oxo-4-morpholinyl]- (9CI) (CA INDEX NAME)

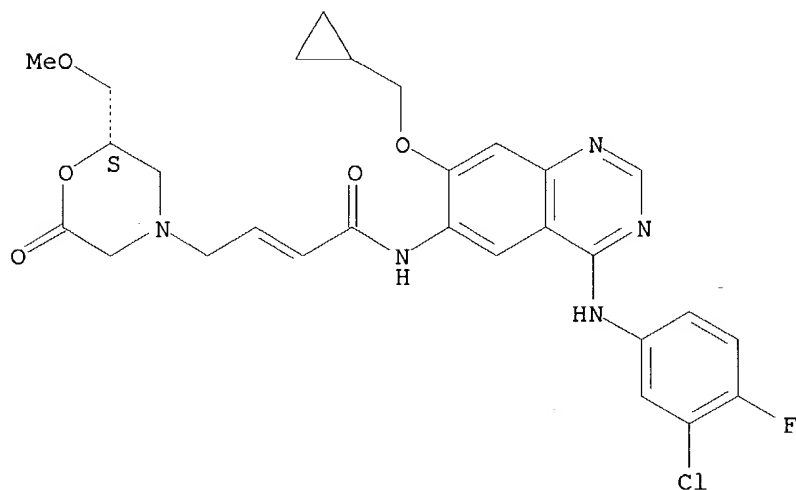
09/938,235

Absolute stereochemistry.
Double bond geometry unknown.

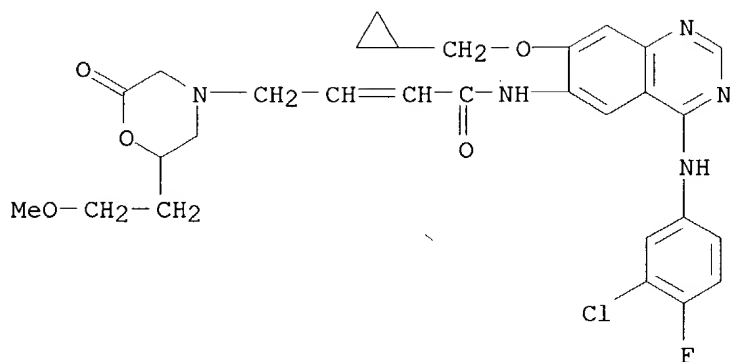


RN 402570-00-7 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[(2S)-2-(methoxymethyl)-6-oxo-4-morpholinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



RN 402570-01-8 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[2-(2-methoxyethyl)-6-oxo-4-morpholinyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 6 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:171891 CAPLUS

DOCUMENT NUMBER: 136:216761

TITLE: Preparation of 4-amino-6-vinylcarbonylaminoquinazoline
s as epidermal growth factor receptor signal
transduction inhibitors

INVENTOR(S): Himmelsbach, Frank; Langkopf, Elke; Jung, Birgit;
Blech, Stefan; Solca, Flavio

PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma Kg, Germany

SOURCE: PCT Int. Appl., 52 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

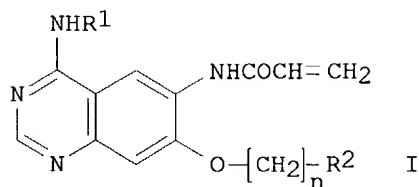
PATENT INFORMATION:

assigned
1. At 946
6,403,580

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002018375	A1	20020307	WO 2001-EP9534	20010818
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10042064	A1	20020307	DE 2000-10042064	20000826
AU 2002010444	A5	20020313	AU 2002-10444	20010818
EP 1322645	A2	20030702	EP 2001-978279	20010818
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004507537	T2	20040311	JP 2002-523890	20010818
US 6403580	B1	20020611	US 2001-935498	20010823
PRIORITY APPLN. INFO.:			DE 2000-10042064	A 20000826
			US 2000-230541P	P 20000905
			WO 2001-EP9534	W 20010818

OTHER SOURCE(S): MARPAT 136:216761

GI



AB Title compds. [I; R1 = PhCH2, 1-phenylethyl, (substituted) Ph; R2 = N-(2-oxotetrahydrofuran-4-yl)methylamino, N(CH2CO2R3)2, (substituted) R4OCOCH2NCH2CH2OH, 2-oxomorpholin-4-yl; R3 = H, Me, Et; R4 = H, alkyl; n = 2-4], were prepared. Thus, a mixture of CH2:CHCO2H and Et3N was stirred for 1 h at -50° with CH2:CHCO2Cl in THF followed by addition of 6-amino-4-[(3-chloro-4-fluorophenyl)amino]-7-[3-(2,2-dimethyl-6-oxomorpholin-4-yl)propyloxy]quinazoline (preparation given) in THF at -55° and slowly heating up at 0° up to completely conversion to give 60% 4-[(3-chloro-4-fluorophenyl)amino]-7-[3-(2,2-dimethyl-6-oxomorpholin-4-yl)propyloxy]-6-[(vinylcarbonyl)amino]quinazoline. One of the exemplified examples, 4-[(R)-(1-phenylethyl)amino]-7-[2-(2,2-dimethyl-6-oxomorpholin-4-yl)ethoxy]-6-[(vinylcarbonyl)amino]quinazoline, inhibited epidermal growth factor (EGF)-dependent proliferation of F/L-HERc cells with IC50 = 0.4 nM. The invention relates to the use of the title compds. for treating tumor diseases, and lung and respiratory tract disorders.

IT 402724-01-0P 402724-02-1P 402724-05-4P
 402724-09-8P 402724-10-1P 402724-11-2P
 402724-12-3P 402724-14-5P 402724-16-7P
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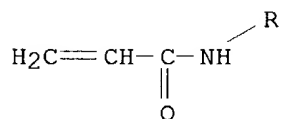
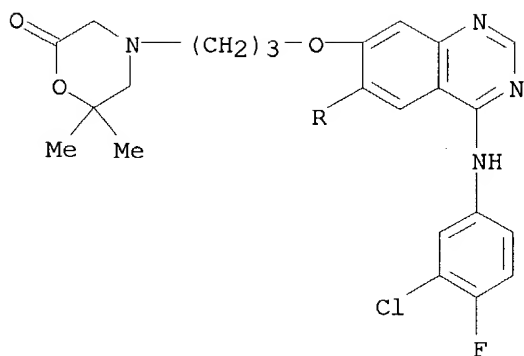
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of (amino)(vinylcarbonylamino)quinazolines as epidermal growth factor receptor signal transduction inhibitors)

RN 402724-01-0 CAPLUS

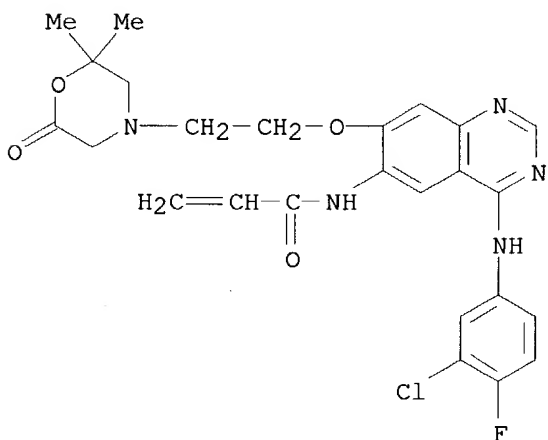
CN 2-Propenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[3-(2,2-dimethyl-6-oxo-4-morpholinyl)propoxy]-6-quinazolinyl]- (9CI) (CA INDEX NAME)

09/938,235



RN 402724-02-1 CAPLUS

CN 2-Propenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[2-(2,2-dimethyl-6-oxo-4-morpholinyl)ethoxy]-6-quinazolinyl]- (9CI) (CA INDEX NAME)

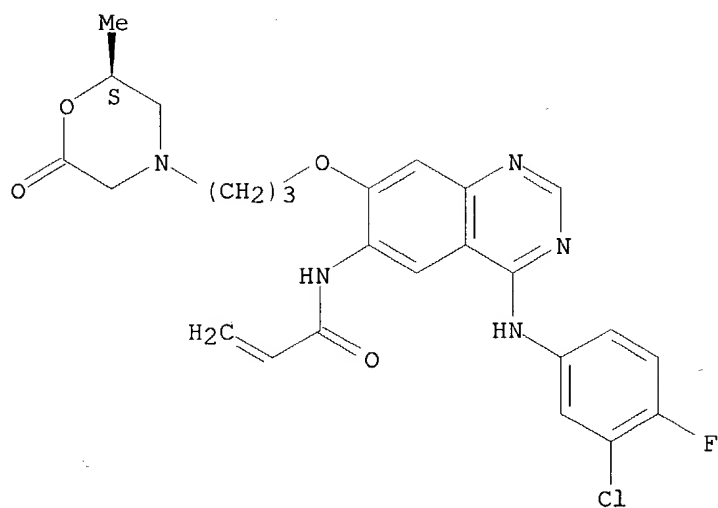


RN 402724-05-4 CAPLUS

CN 2-Propenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[3-[(2S)-2-methyl-6-oxo-4-morpholinyl]propoxy]-6-quinazolinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

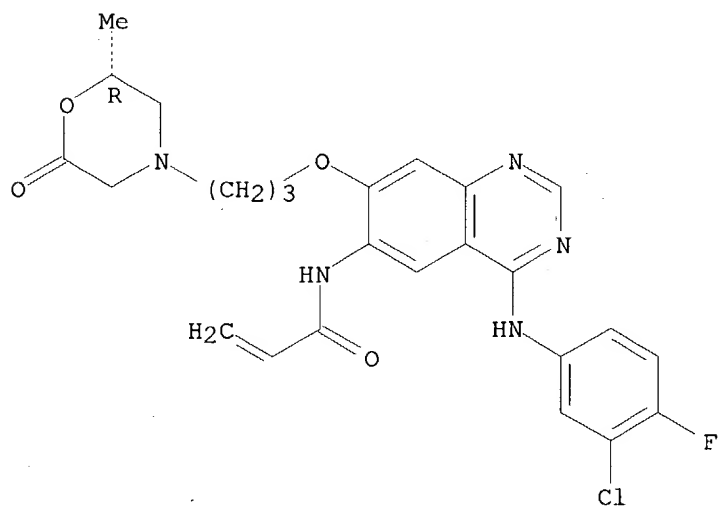
09/938,235



RN 402724-09-8 CAPLUS

CN 2-Propenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[3-[(2R)-2-methyl-6-oxo-4-morpholinyl]propoxy]-6-quinazolinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

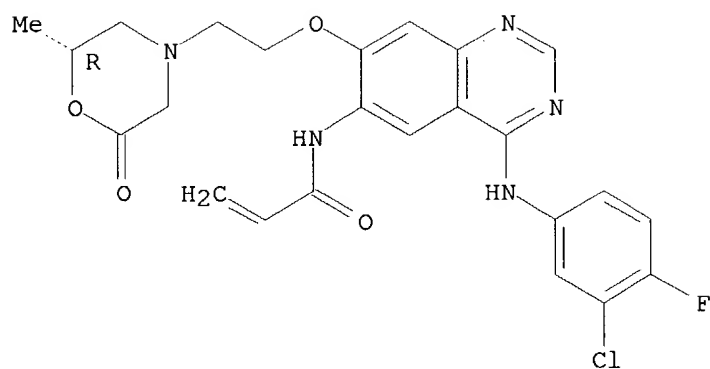


RN 402724-10-1 CAPLUS

CN 2-Propenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[2-[(2R)-2-methyl-6-oxo-4-morpholinyl]ethoxy]-6-quinazolinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

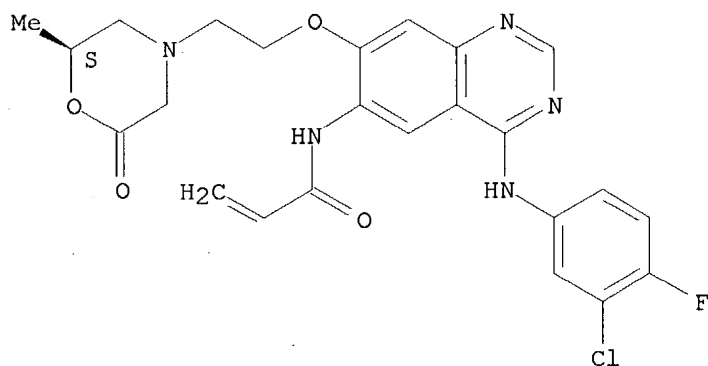
09/938,235



RN 402724-11-2 CAPLUS

CN 2-Propenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[2-[(2S)-2-methyl-6-oxo-4-morpholinyl]ethoxy]-6-quinazolinyl]- (9CI) (CA INDEX NAME)

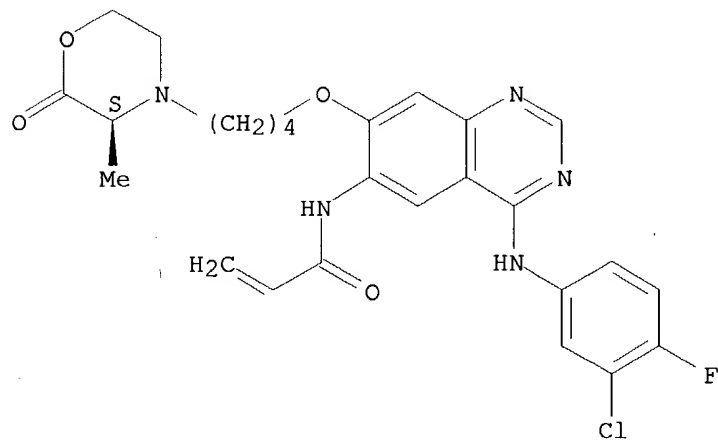
Absolute stereochemistry.



RN 402724-12-3 CAPLUS

CN 2-Propenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[4-[(3S)-3-methyl-2-oxo-4-morpholinyl]butoxy]-6-quinazolinyl]- (9CI) (CA INDEX NAME)

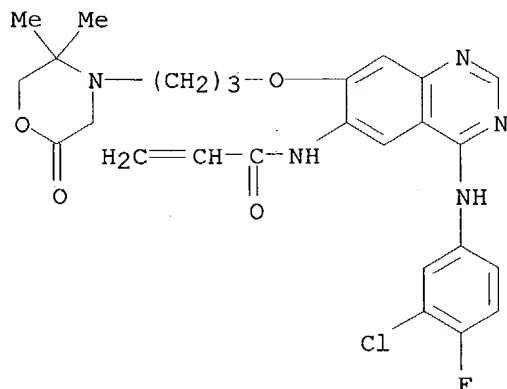
Absolute stereochemistry.



09/938,235

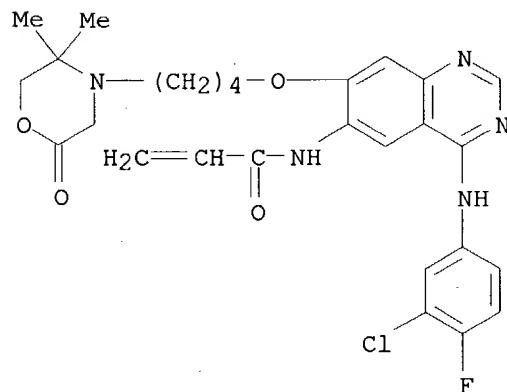
RN 402724-14-5 CAPLUS

CN 2-Propenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[3-(5,5-dimethyl-2-oxo-4-morpholinyl)propoxy]-6-quinazolinyl]- (9CI) (CA INDEX NAME)



RN 402724-16-7 CAPLUS

CN 2-Propenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[4-(5,5-dimethyl-2-oxo-4-morpholinyl)butoxy]-6-quinazolinyl]- (9CI) (CA INDEX NAME)

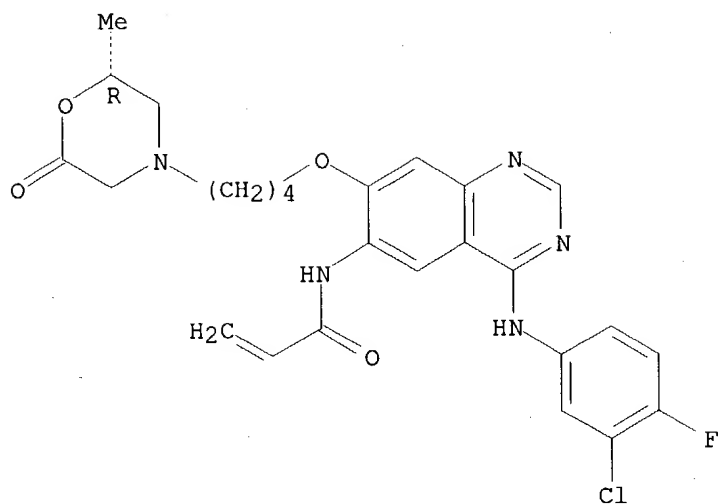


RN 402724-17-8 CAPLUS

CN 2-Propenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[4-[(2R)-2-methyl-6-oxo-4-morpholinyl]butoxy]-6-quinazolinyl]- (9CI) (CA INDEX NAME)

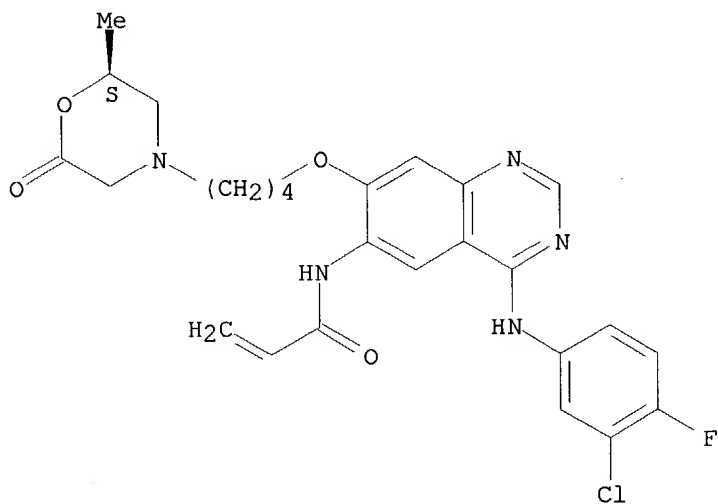
Absolute stereochemistry.

09/938,235

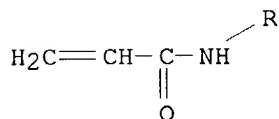
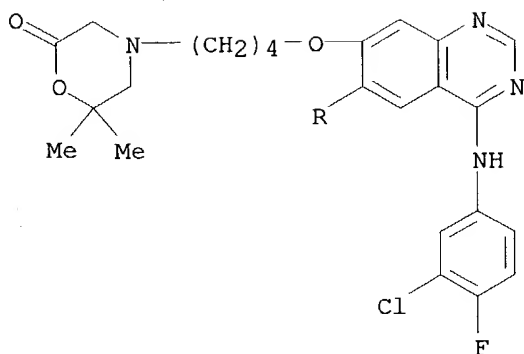


RN 402724-18-9 CAPLUS
CN 2-Propenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[4-[(2S)-2-methyl-6-oxo-4-morpholinyl]butoxy]-6-quinazolinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

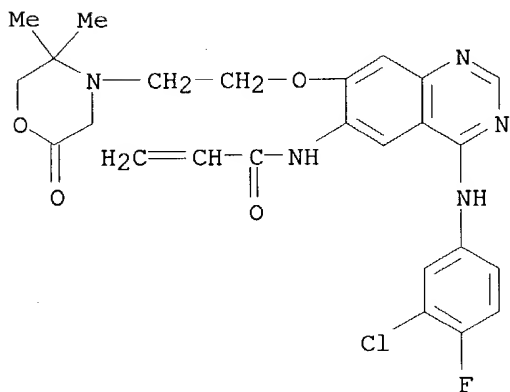


RN 402724-19-0 CAPLUS
CN 2-Propenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[4-(2,2-dimethyl-6-oxo-4-morpholinyl)butoxy]-6-quinazolinyl]- (9CI) (CA INDEX NAME)



RN 402724-21-4 CAPLUS

CN 2-Propenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[2-(5,5-dimethyl-2-oxo-4-morpholinyl)ethoxy]-6-quinazolinyl]- (9CI) (CA INDEX NAME)



IT 402723-54-0P 402723-55-1P 402723-56-2P
 402723-58-4P 402723-60-8P 402723-61-9P
 402723-62-0P 402723-63-1P 402723-66-4P
 402723-68-6P 402723-70-0P 402723-83-5P
 402723-85-7P 402723-86-8P 402723-87-9P
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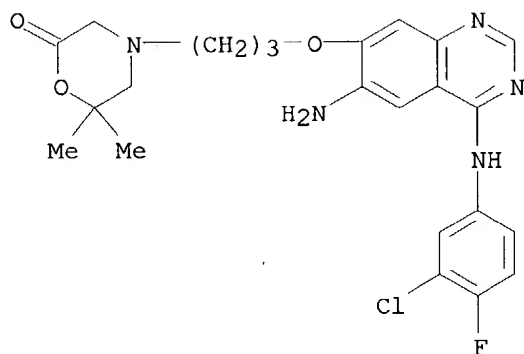
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of (amino) (vinylcarbonylamino)quinazolines as epidermal growth factor receptor signal transduction inhibitors)

RN 402723-54-0 CAPLUS

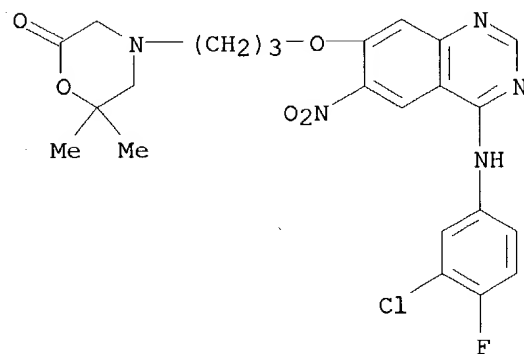
CN 2-Morpholinone, 4-[3-[[6-amino-4-[(3-chloro-4-fluorophenyl)amino]-7-quinazolinyl]oxy]propyl]-6,6-dimethyl- (9CI) (CA INDEX NAME)

09/938,235



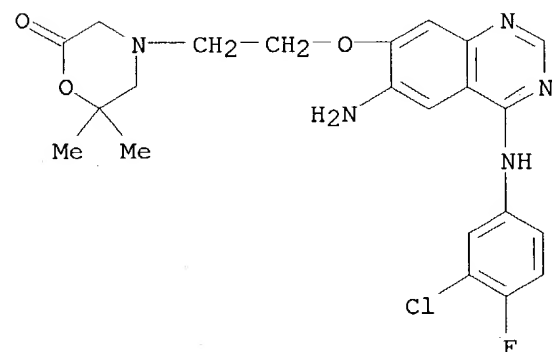
RN 402723-55-1 CAPLUS

CN 2-Morpholinone, 4-[3-[[4-[(3-chloro-4-fluorophenyl)amino]-6-nitro-7-quinazolinyl]oxy]propyl]-6,6-dimethyl- (9CI) (CA INDEX NAME)



RN 402723-56-2 CAPLUS

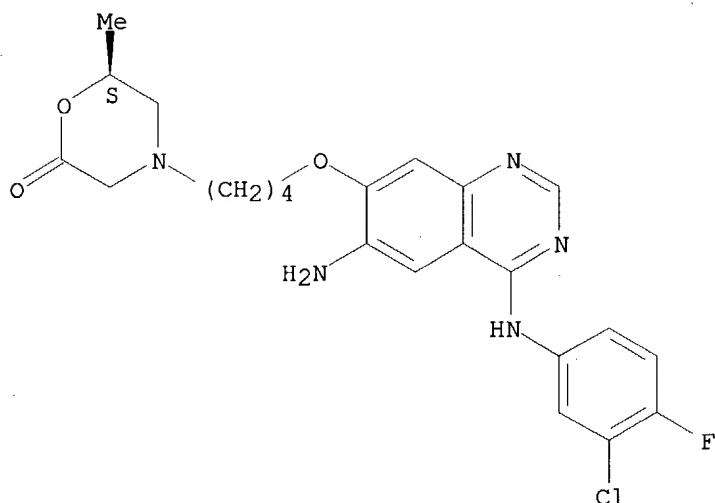
CN 2-Morpholinone, 4-[2-[[6-amino-4-[(3-chloro-4-fluorophenyl)amino]-7-quinazolinyl]oxy]ethyl]-6,6-dimethyl- (9CI) (CA INDEX NAME)



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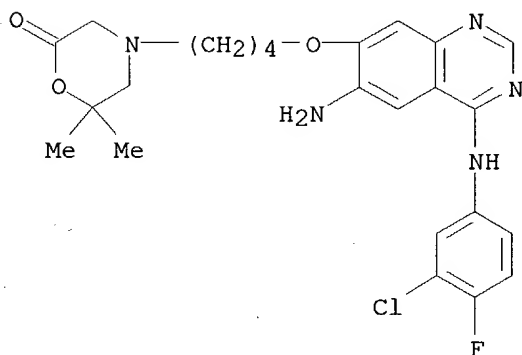
CN 2-Morpholinone, 4-[3-[[6-amino-4-[(3-chloro-4-fluorophenyl)amino]-7-quinazolinyl]oxy]propyl]-6-methyl-, (6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 402723-99-3 CAPLUS

CN 2-Morpholinone, 4-[4-[[6-amino-4-[(3-chloro-4-fluorophenyl)amino]-7-quinazolinyl]oxy]butyl]-6,6-dimethyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 7 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:171889 CAPLUS

DOCUMENT NUMBER: 136:232315

TITLE: Preparation of 4-amino-6-vinylcarbonylaminoquinazoline
s as epidermal growth factor receptor signal
transduction inhibitors

INVENTOR(S): Himmelsbach, Frank; Langkopf, Elke; Jung, Birgit;
Blech, Stefan; Solca, Flavio

PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma Kg, Germany

SOURCE: PCT Int. Appl., 78 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE

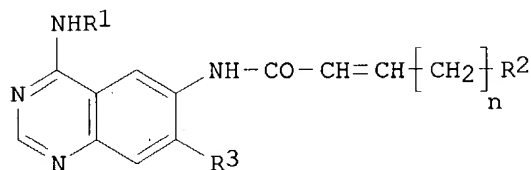
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6,653,305

WO 2002018373	A1	20020307	WO 2001-EP9537	20010818
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US 2002077330	A1	20020620	US 2001-929931	20010815
US 6653305	B2	20031125		
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EP 1315717	A1	20030604	EP 2001-962953	20010818
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
JP 2004517048	T2	20040610	JP 2002-523888	20010818
PRIORITY APPLN. INFO.:			DE 2000-10042060	A 20000826
			US 2000-230389P	P 20000906
			WO 2001-EP9537	W 20010818

OTHER SOURCE(S): MARPAT 136:232315
GI



AB Title compds. [I; R1 = PhCH₂, 1-phenylethyl, (substituted) Ph; R2 = N-[(1,3-dioxolan-2-yl)methyl]methylamino, (substituted) R₄OCOCH₂NCH₂CH₂OH, 2-oxomorpholin-4-yl; R₄ = H, alkyl; R₃ = H, (alkoxy)alkoxy, cycloalkylalkoxy, tetrahydrofuran-3-yloxy, tetrahydropyran-3-yloxy, tetrahydropyran-4-yloxy, tetrahydrofuranylmethoxy, tetrahydropyranylmethoxy; n = 1-3], were prepared Thus, a mixture of 6-amino-4-[(3-chloro-4-fluorophenyl)amino]-7-cyclopropylmethoxyquinazoline (preparation given) and disopropylethylamine in THF was dropwise treated under ice-cooling with BrCH₂CH:CHCO₂Cl (preparation given) in CH₂Cl₂ followed by stirring for 1 h under ice-cooling and for 2 h at room temperature and addition of

(S)-(2-hydroxypropylamino)acetic acid tert-Bu ester in CH₂Cl₂ to give after stirring over night at room temperature and stirring for 5 h at 60° 64% 4-[(3-chloro-4-fluorophenyl)amino]-6-[(4-[N-(tert-butyloxycarbonylmethyl)-N-((S)-2-hydroxyprop-1-yl)amino]-1-oxo-2-buten-1-yl)amino]-7-cyclopropylmethoxyquinazoline. Several I inhibited epidermal growth factor (EGF)-dependent proliferation of F/L-HERc cells with IC₅₀ = 0.02-15 nM. The invention relates to the use of the title compds. for treating tumor diseases, and lung and respiratory tract disorders.

IT 402855-53-2P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of (amino)(vinylcarbonylamino)quinazolines as epidermal growth factor receptor signal transduction inhibitors)

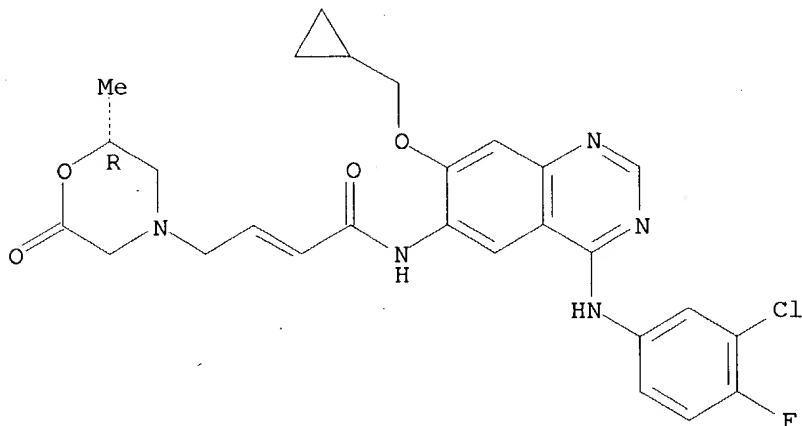
09/938,235

RN 402855-53-2 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[(2R)-2-methyl-6-oxo-4-morpholinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.



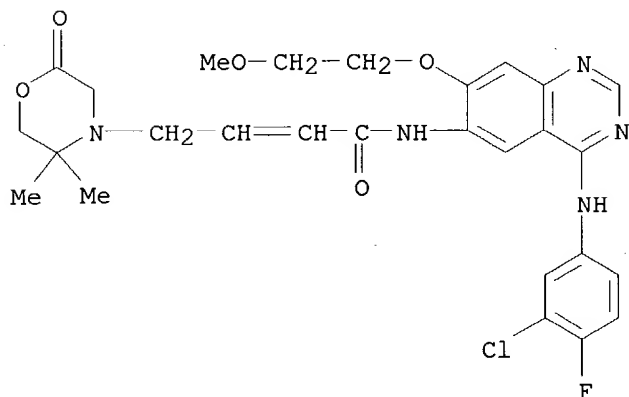
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402855-67-8P 402855-70-3P 402855-71-4P
402855-72-5P 402855-73-6P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

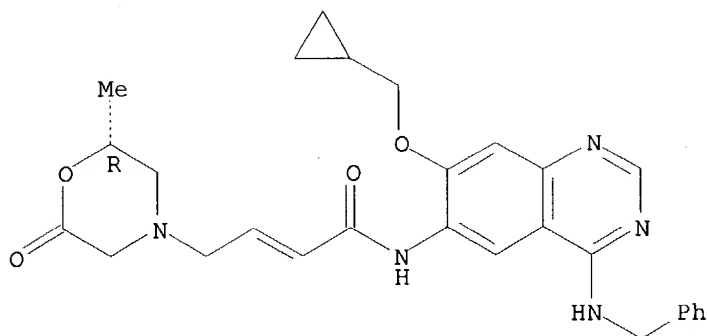
(preparation of (amino)(vinylcarbonylamino)quinazolines as epidermal growth factor receptor signal transduction inhibitors)

RN 402855-19-0 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(2-methoxyethoxy)-6-quinazolinyl]-4-(5,5-dimethyl-2-oxo-4-morpholinyl)- (9CI) (CA INDEX NAME)

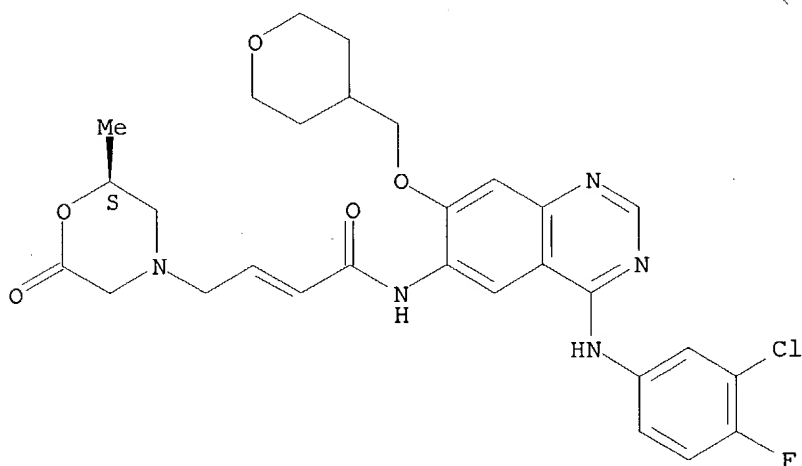


09/938,235



RN 402855-73-6 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[(tetrahydro-2H-pyran-4-yl)methoxy]-6-quinazolinyl]-4-[(2S)-2-methyl-6-oxo-4-morpholinyl]-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 8 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:171888 CAPLUS

DOCUMENT NUMBER: 136:216759

TITLE: Preparation of aminoquinazolines as epidermal growth factor receptor signal transduction inhibitors

INVENTOR(S): Himmelsbach, Frank; Langkopf, Elke; Jung, Birgit; Blech, Stefan; Solca, Flavio

PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma Kg, Germany

SOURCE: PCT Int. Appl., 95 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

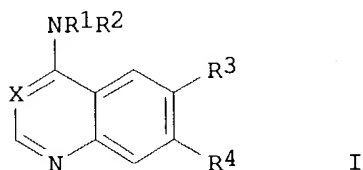
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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assigned
6,617,329
d.f. 94.6

WO 2002018372 A1 20020307 WO 2001-EP9533 20010818
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CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL,
PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG,
US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
DE 10042059 A1 20020307 DE 2000-10042059 20000826
AU 2001095481 A5 20020313 AU 2001-95481 20010818
EP 1315718 A1 20030604 EP 2001-976107 20010818
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IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
JP 2004507535 T2 20040311 JP 2002-523887 20010818
US 2002049197 A1 20020425 US 2001-938314 20010823
US 6617329 B2 20030909
PRIORITY APPLN. INFO.: DE 2000-10042059 A 20000826
US 2000-230118P P 20000905
WO 2001-EP9533 W 20010818
OTHER SOURCE(S): MARPAT 136:216759
GI



AB Title compds. [I; X = N, (substituted) methynyl; R1 = H, Me; R2 = (substituted) Ph, PhCH2, 1-phenylethyl; R3, R4 = AB, CD; A = (oxy)alkenyl, O; B = (substituted) pyrrolidinyl, piperidinyl, hexahydroazepinyl, piperazinyl, 2-oxomorpholin-4-yl, etc.; C = oxyalkenyl, O; D = (substituted) amino, alkenylimino, imidazolyl, heterocycloalkyl, alkoxy, cycloalkoxy, cycloalkylalkoxy, tetrahydrofuran-3-yloxy, tetrahydropyran-3-yloxy, tetrahydropyran-4-yloxy, tetrahydrofuranylmethoxy, tetrahydropyranylmethoxy, etc.; or CD = H], were prepared Thus, 4-[(3-chloro-4-fluorophenyl)amino]-6-cyclopentyloxy-7-[2-(piperazin-1-yl)ethoxy]quinazoline (preparation given) in MeCN was refluxed for 4 h with K2CO3, NaI, and (R)-5-[(methanesulfonyloxy)methyl]-2-oxotetrahydrofuran followed by addition of (R)-5-[(methanesulfonyloxy)methyl]-2-oxotetrahydrofuran and reflux for 15 h to give 47% 4-[(3-chloro-4-fluorophenyl)amino]-6-cyclopentyloxy-7-[2-(4-[(R)-(2-oxotetrahydrofuran-5-yl)methyl]piperazin-1-yl)ethoxy]quinazoline. Several I inhibited epidermal growth factor (EGF)-dependent proliferation of F/L-HERc cells with IC50 = 4-67 nM. The invention relates to the use of the title compds. for treating tumor diseases, and lung and respiratory tract disorders.

IT **402573-59-5P 402573-60-8P**

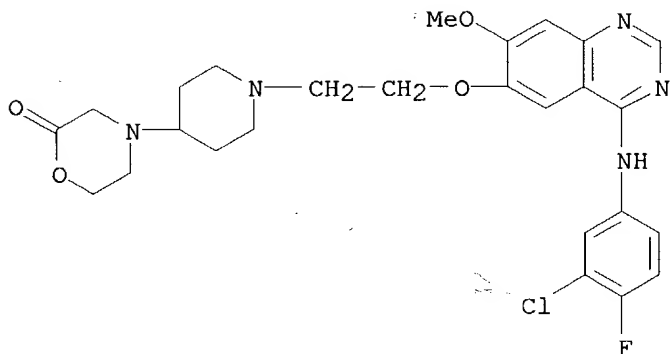
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of aminoquinazolines as epidermal growth factor receptor signal transduction inhibitors)

RN 402573-59-5 CAPLUS

09/938,235

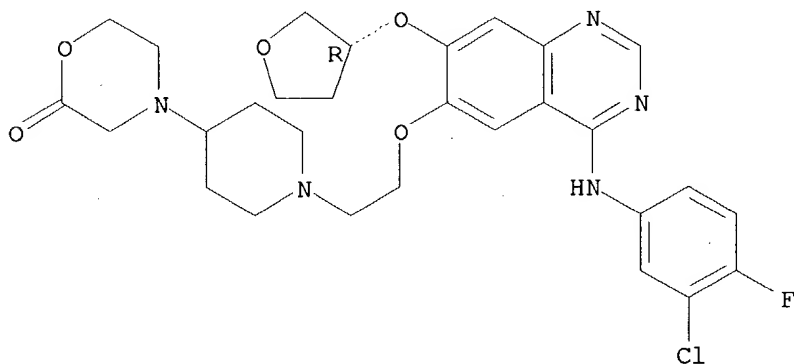
CN 2-Morpholinone, 4-[1-[2-[[4-[(3-chloro-4-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]ethyl]-4-piperidinyl]- (9CI) (CA INDEX NAME)



RN 402573-60-8 CAPLUS

CN 2-Morpholinone, 4-[1-[2-[[4-[(3-chloro-4-fluorophenyl)amino]-7-[(3R)-tetrahydro-3-furanyl]oxy]-6-quinazolinyl]oxy]ethyl]-4-piperidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 9 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:171867 CAPLUS

DOCUMENT NUMBER: 136:232314

TITLE: Preparation of aminoquinazolines as epidermal growth factor receptor signal transduction inhibitors

INVENTOR(S): Himmelsbach, Frank; Langkopf, Elke; Jung, Birgit; Blech, Stefan; Solca, Flavio

PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma Kg, Germany

SOURCE: PCT Int. Appl., 103 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

assiam
6,656,946

PATENT NO.

KIND

DATE

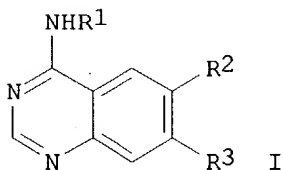
APPLICATION NO.

DATE

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NO 2003000870	A	20030225	NO 2003-870	20030225
PRIORITY APPLN. INFO.:			DE 2000-10042058	A 20000826
			US 2000-230035P	P 20000905
			WO 2001-EP9532	W 20010818

OTHER SOURCE(S): MARPAT 136:232314

GI



AB Title compds. [I; R¹ = PhCH₂, 1-phenylethyl, (substituted) Ph; R², R³ = O(CH₂)_mR⁴, methoxy, cyclobutyloxy, cyclopentyloxy, cyclopropylmethoxy, cyclobutylmethoxy, cyclopentylmethoxy, tetrahydrofuran-3-yloxy, tetrahydropyran-3-yloxy, tetrahydropyran-4-yloxy, tetrahydrofuranylmethoxy, tetrahydropyranylmethoxy; R⁴ = N-(2-oxotetrahydrofuran-4-yl)methylamino, N-(2-oxotetrahydrofuran-4-yl)ethylamino, (substituted) 2-oxo-morpholin-4-yl, R⁵OCOCH₂NCH₂CH₂OH; R⁵ = H, alkyl; m = 2-4], were prepared. Thus, 4-[(3-bromophenyl)amino]-6-[2-(N-[(tert-butyloxycarbonyl)methyl]-N-((S)-2-hydroxypropyl)amino)ethoxy]-7-methoxyquinazoline (preparation given) in MeCN was stirred under reflux with MeSO₂OH for 3 h followed by addition of MeSO₂OH up to completely conversion to give 85% 4-[(3-bromophenyl)amino]-6-[2-((S)-6-methyl-2-oxomorpholin-4-yl)ethoxy]-7-methoxyquinoline. Tested I inhibited epidermal growth factor (EGF)-dependent proliferation of F/L-HERc cells with IC₅₀ = 29-59 nM. The invention relates to the use of the title compds. for treating tumor diseases, and lung and respiratory tract disorders.

IT 402734-57-0P 402734-58-1P 402734-59-2P
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 402734-67-2P 402734-68-3P 402734-69-4P
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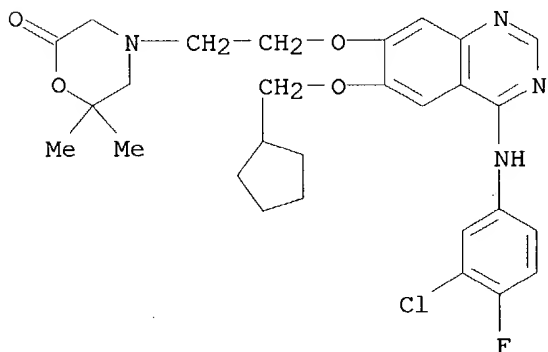
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 402735-13-1P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
 (Uses)

(preparation of aminoquinazolines as epidermal growth factor receptor signal
 transduction inhibitors)

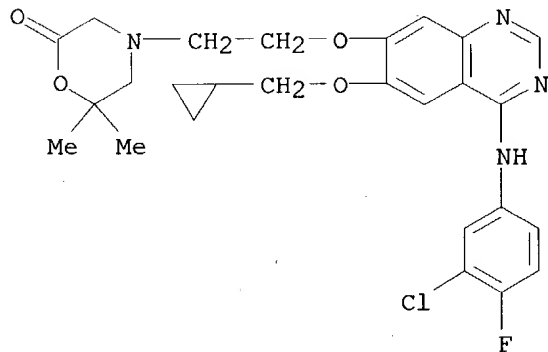
RN 402734-57-0 CAPLUS

CN 2-Morpholinone, 4-[2-[[4-[(3-chloro-4-fluorophenyl)amino]-6-
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RN 402734-58-1 CAPLUS

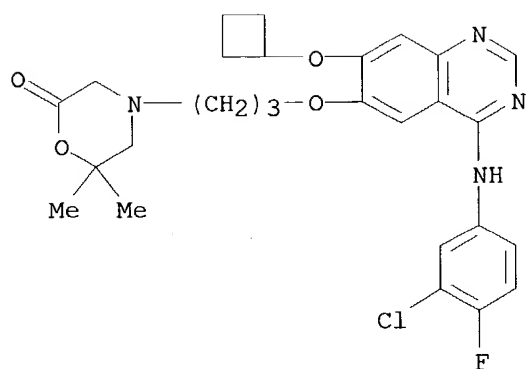
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 INDEX NAME)



RN 402734-59-2 CAPLUS

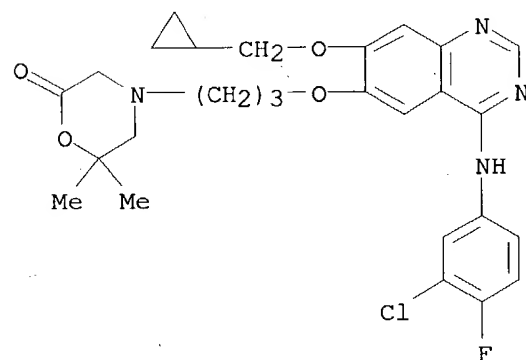
CN 2-Morpholinone, 4-[3-[[4-[(3-chloro-4-fluorophenyl)amino]-7-
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 NAME)

09/938,235



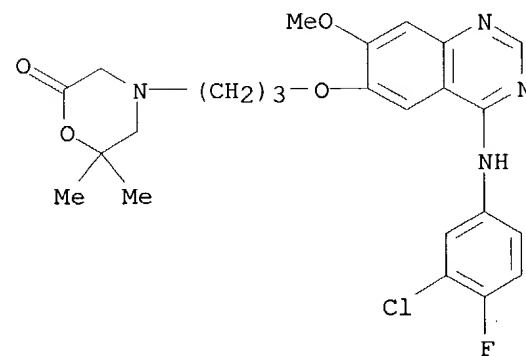
RN 402734-60-5 CAPLUS

CN 2-Morpholinone, 4-[3-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]oxy]propyl]-6,6-dimethyl- (9CI) (CA INDEX NAME)



RN 402734-61-6 CAPLUS

CN 2-Morpholinone, 4-[3-[[4-[(3-chloro-4-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]propyl]-6,6-dimethyl- (9CI) (CA INDEX NAME)

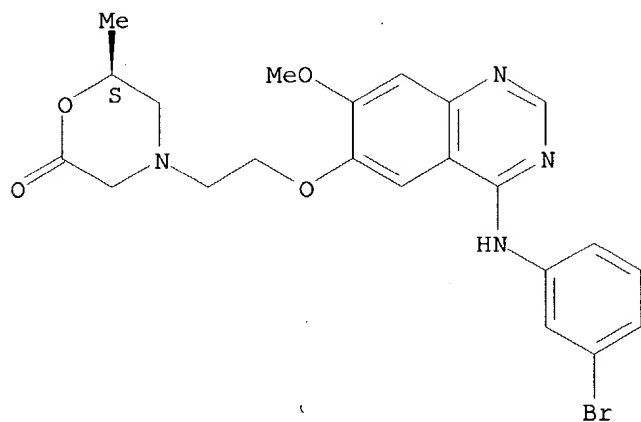


RN 402734-65-0 CAPLUS

CN 2-Morpholinone, 4-[2-[[4-[(3-bromophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]ethyl]-6-methyl-, (6S)- (9CI) (CA INDEX NAME)

09/938,235

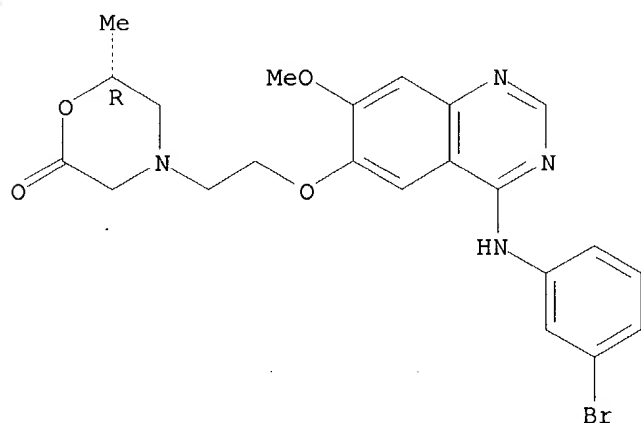
Absolute stereochemistry.



RN 402734-67-2 CAPLUS

CN 2-Morpholinone, 4-[2-[[4-[(3-bromophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]ethyl]-6-methyl-, (6R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

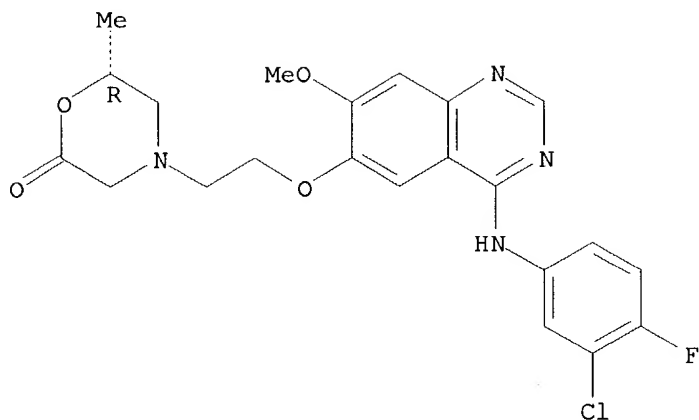


RN 402734-68-3 CAPLUS

CN 2-Morpholinone, 4-[2-[[4-[(3-chloro-4-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]ethyl]-6-methyl-, (6R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

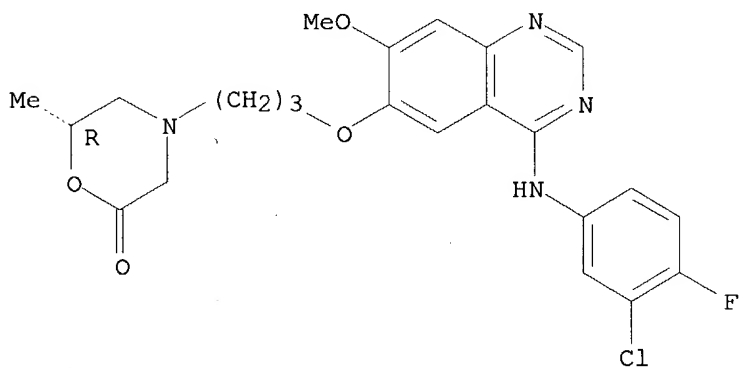
09/938,235



RN 402734-69-4 CAPLUS

CN 2-Morpholinone, 4-[3-[[4-[(3-chloro-4-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]propyl]-6-methyl-, (6R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

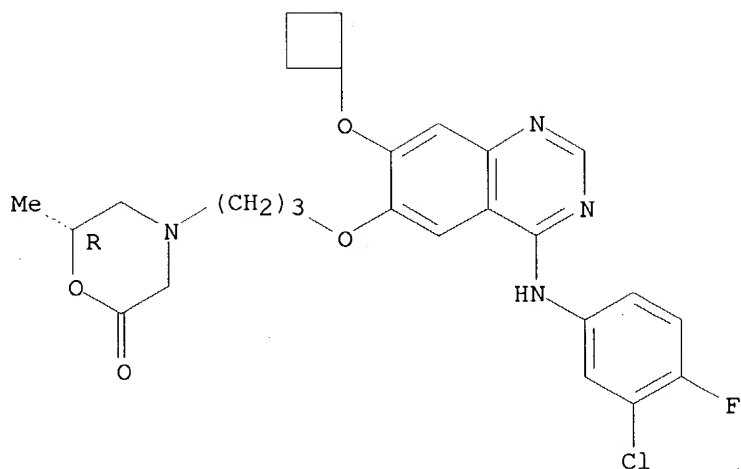


RN 402734-72-9 CAPLUS

CN 2-Morpholinone, 4-[3-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclobutyloxy)-6-quinazolinyl]oxy]propyl]-6-methyl-, (6R)- (9CI) (CA INDEX NAME)

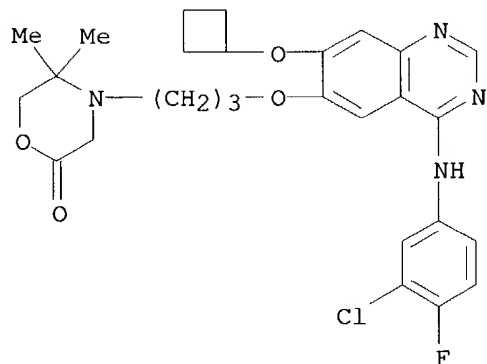
Absolute stereochemistry.

09/938,235



RN 402734-73-0 CAPLUS

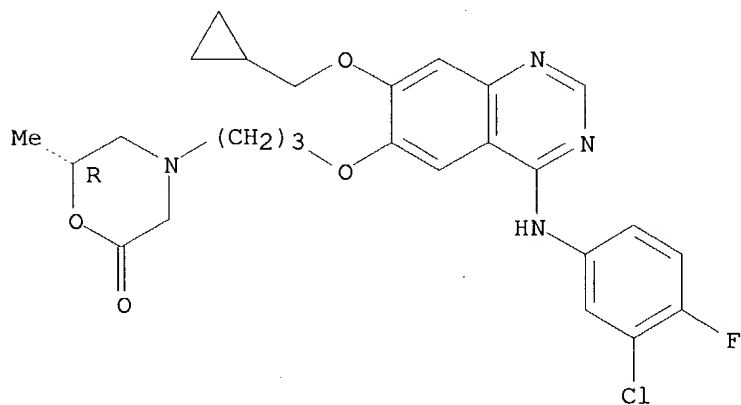
CN 2-Morpholinone, 4-[3-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclobutylloxy)-6-quinazolinyl]oxy]propyl]-5,5-dimethyl- (9CI) (CA INDEX NAME)



RN 402734-74-1 CAPLUS

CN 2-Morpholinone, 4-[3-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]oxy]propyl]-6-methyl-, (6R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

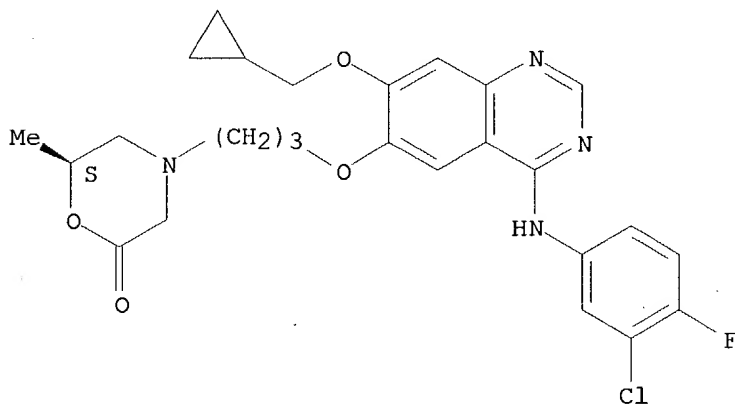


09/938,235

RN 402734-75-2 CAPLUS

CN 2-Morpholinone, 4-[3-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]oxy]propyl]-6-methyl-, (6S)- (9CI)
(CA INDEX NAME)

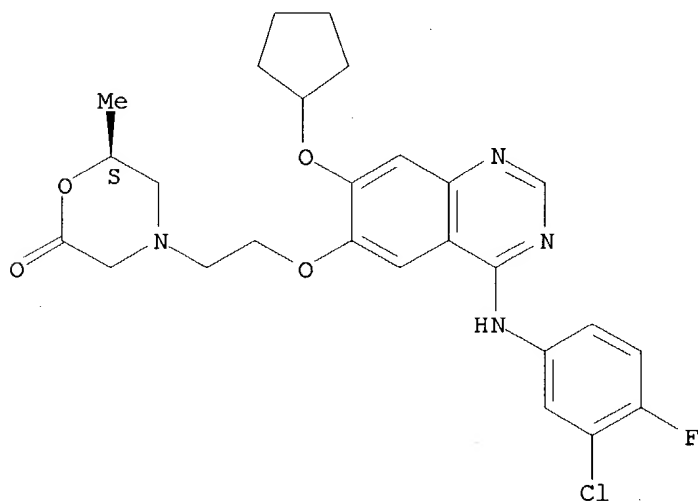
Absolute stereochemistry.



RN 402734-76-3 CAPLUS

CN 2-Morpholinone, 4-[2-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopentyloxy)-6-quinazolinyl]oxy]ethyl]-6-methyl-, (6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

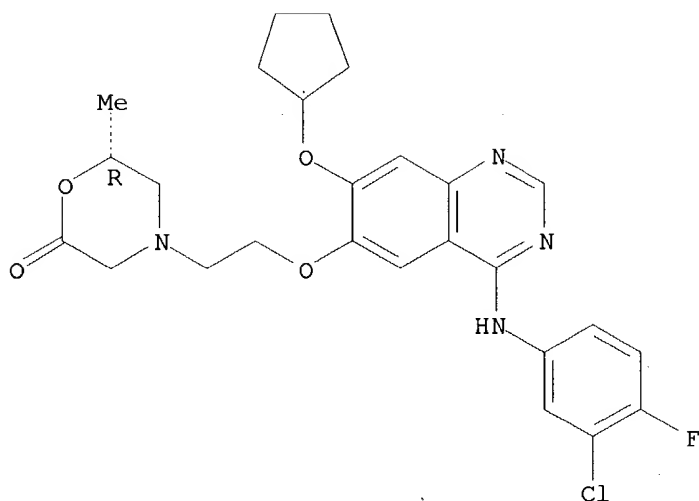


RN 402734-77-4 CAPLUS

CN 2-Morpholinone, 4-[2-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopentyloxy)-6-quinazolinyl]oxy]ethyl]-6-methyl-, (6R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

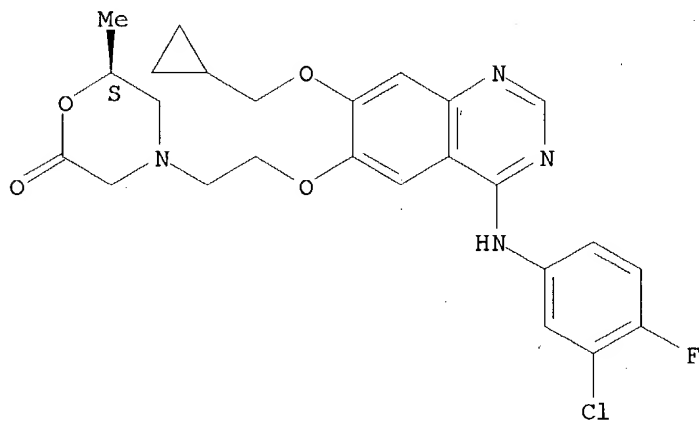
09/938,235



RN 402734-79-6 CAPLUS

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Absolute stereochemistry.

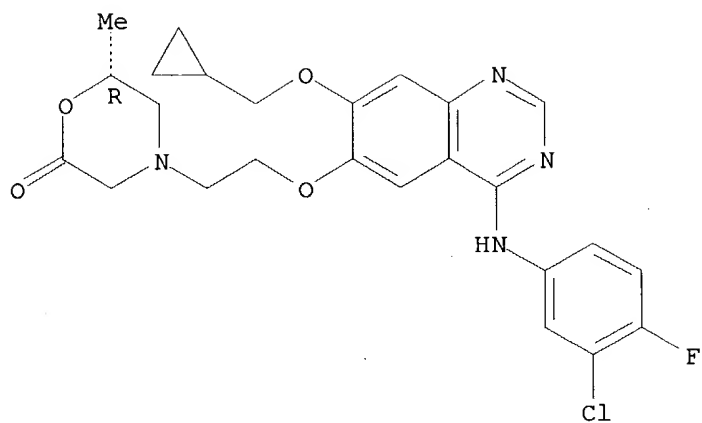


RN 402734-80-9 CAPLUS

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Absolute stereochemistry.

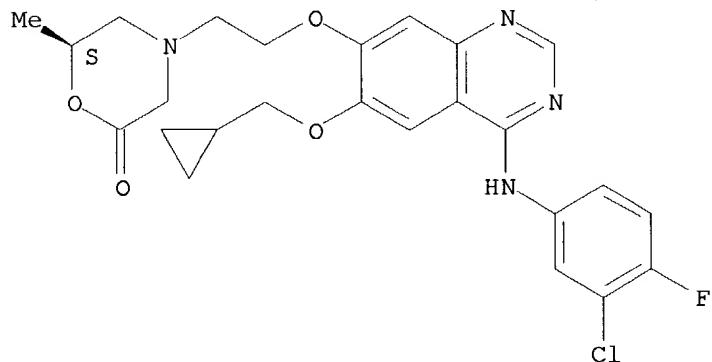
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RN 402734-82-1 CAPLUS

CN 2-Morpholinone, 4-[2-[[4-[(3-chloro-4-fluorophenyl)amino]-6-(cyclopropylmethoxy)-7-quinazolinyl]oxy]ethyl]-6-methyl-, (6S)- (9CI) (CA INDEX NAME)

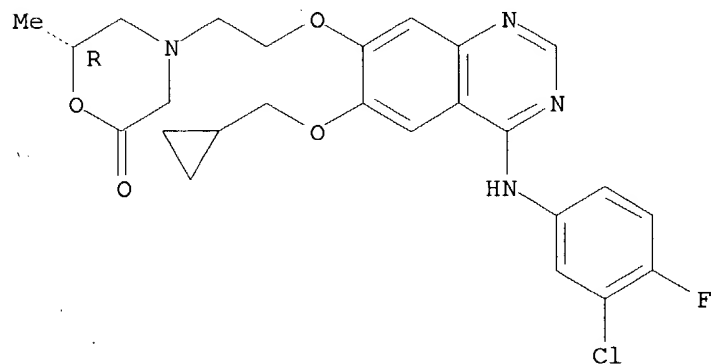
Absolute stereochemistry.



RN 402734-84-3 CAPLUS

CN 2-Morpholinone, 4-[2-[[4-[(3-chloro-4-fluorophenyl)amino]-6-(cyclopropylmethoxy)-7-quinazolinyl]oxy]ethyl]-6-methyl-, (6R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

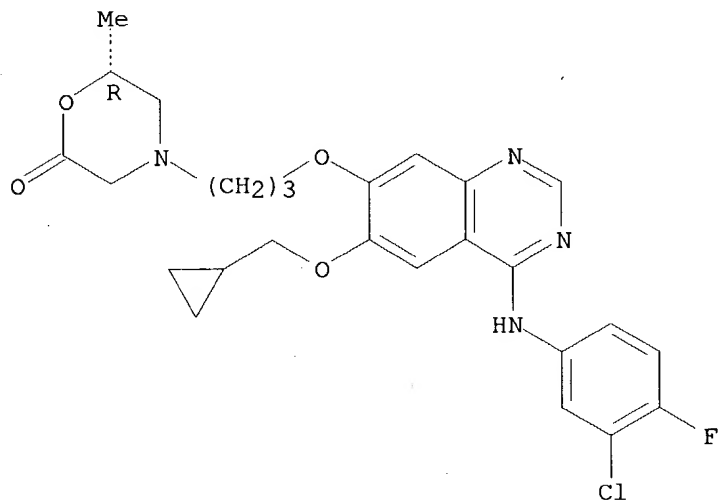


09/938,235

RN 402734-86-5 CAPLUS

CN 2-Morpholinone, 4-[3-[[4-[(3-chloro-4-fluorophenyl)amino]-6-(cyclopropylmethoxy)-7-quinazolinyl]oxy]propyl]-6-methyl-, (6R)- (9CI)
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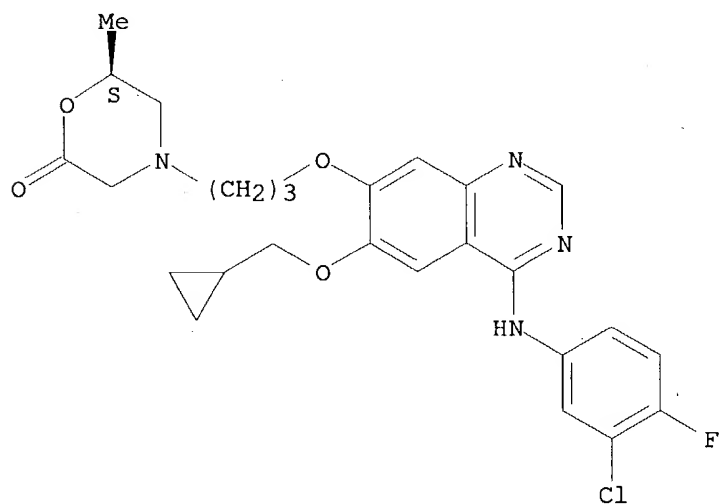
Absolute stereochemistry.



RN 402734-90-1 CAPLUS

CN 2-Morpholinone, 4-[3-[[4-[(3-chloro-4-fluorophenyl)amino]-6-(cyclopropylmethoxy)-7-quinazolinyl]oxy]propyl]-6-methyl-, (6S)- (9CI)
(CA INDEX NAME)

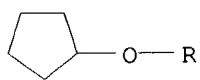
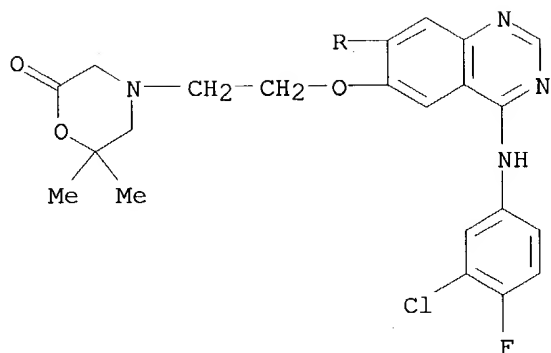
Absolute stereochemistry.



RN 402734-92-3 CAPLUS

CN 2-Morpholinone, 4-[2-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopentylloxy)-6-quinazolinyl]oxy]ethyl]-6,6-dimethyl- (9CI) (CA INDEX NAME)

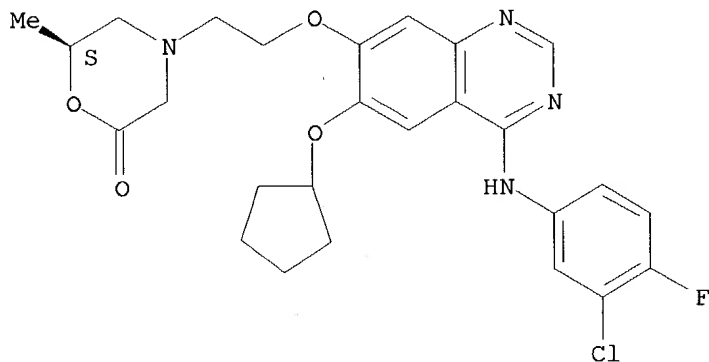
09/938,235



RN 402734-94-5 CAPLUS

CN 2-Morpholinone, 4-[2-[[4-[(3-chloro-4-fluorophenyl)amino]-6-(cyclopentyloxy)-7-quinazolinyl]oxy]ethyl]-6-methyl-, (6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

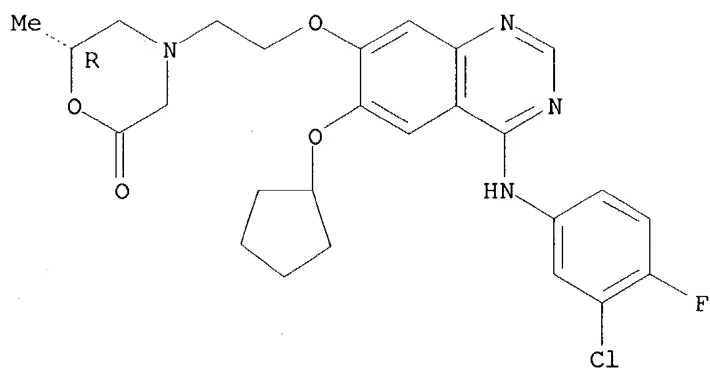


RN 402734-95-6 CAPLUS

CN 2-Morpholinone, 4-[2-[[4-[(3-chloro-4-fluorophenyl)amino]-6-(cyclopentyloxy)-7-quinazolinyl]oxy]ethyl]-6-methyl-, (6R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

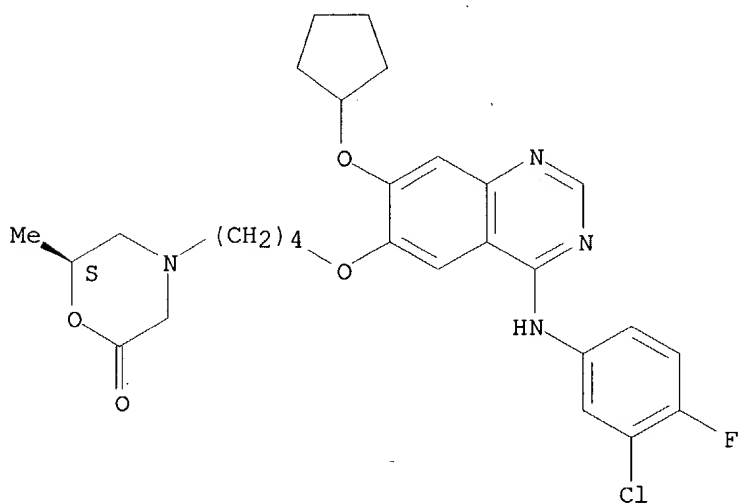
09/938,235



RN 402734-97-8 CAPLUS

CN 2-Morpholinone, 4-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopentyloxy)-6-quinazolinyl]oxy]butyl]-6-methyl-, (6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

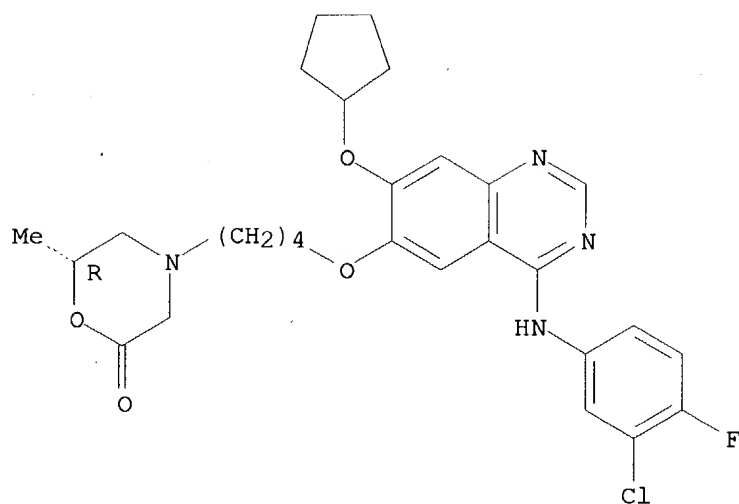


RN 402734-99-0 CAPLUS

CN 2-Morpholinone, 4-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopentyloxy)-6-quinazolinyl]oxy]butyl]-6-methyl-, (6R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

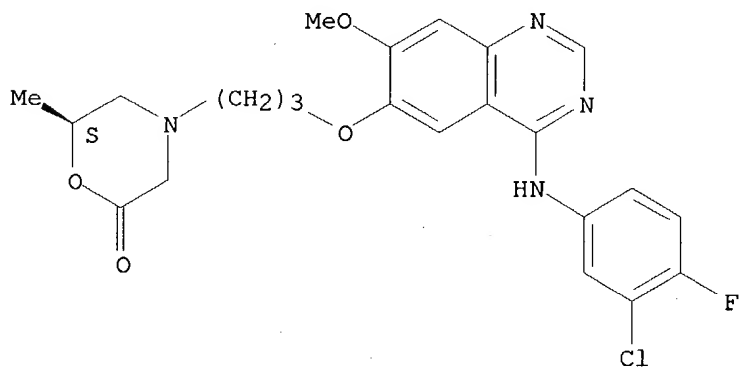
09/938,235



RN 402735-01-7 CAPLUS

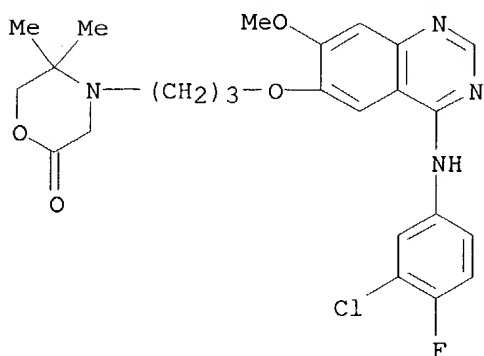
CN 2-Morpholinone, 4-[3-[[4-[(3-chloro-4-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]propyl]-6-methyl-, (6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 402735-02-8 CAPLUS

CN 2-Morpholinone, 4-[3-[[4-[(3-chloro-4-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]propyl]-5,5-dimethyl-, (9CI) (CA INDEX NAME)

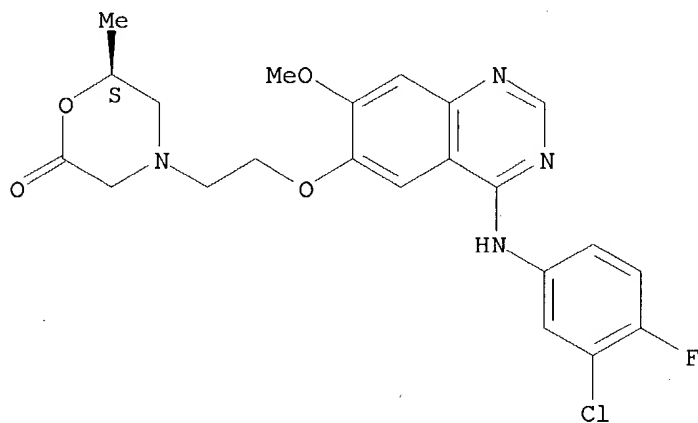


09/938,235

RN 402735-03-9 CAPLUS

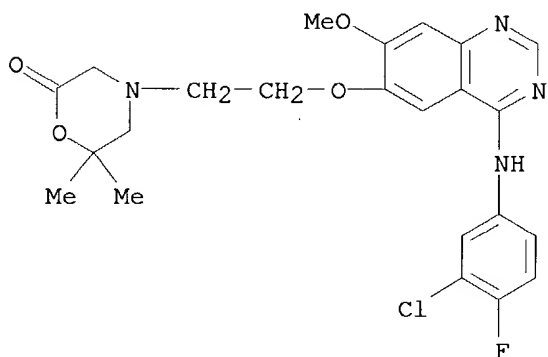
CN 2-Morpholinone, 4-[2-[[4-[(3-chloro-4-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]ethyl]-6-methyl-, (6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 402735-06-2 CAPLUS

CN 2-Morpholinone, 4-[2-[[4-[(3-chloro-4-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]ethyl]-6,6-dimethyl- (9CI) (CA INDEX NAME)

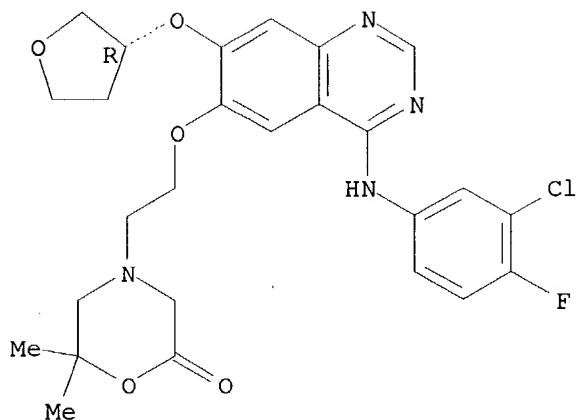


RN 402735-08-4 CAPLUS

CN 2-Morpholinone, 4-[2-[[4-[(3-chloro-4-fluorophenyl)amino]-7-[[[(3R)-tetrahydro-3-furanyl]oxy]-6-quinazolinyl]oxy]ethyl]-6,6-dimethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

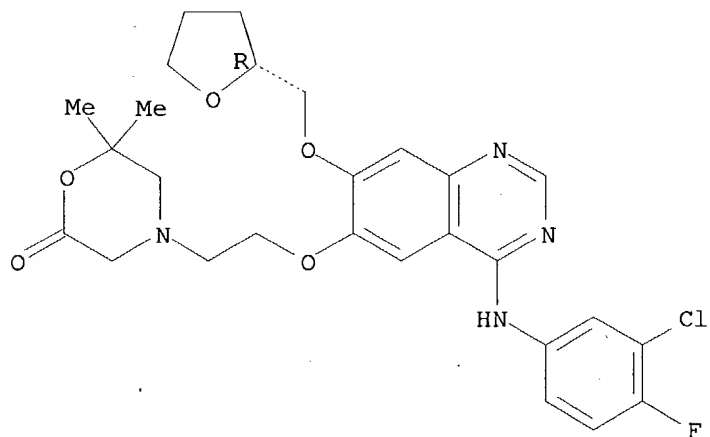
09/938,235



RN 402735-09-5 CAPLUS

CN 2-Morpholinone, 4-[2-[[4-[(3-chloro-4-fluorophenyl)amino]-7-[(2R)-tetrahydro-2-furanyl]methoxy]-6-quinazolinyl]oxy]ethyl]-6,6-dimethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

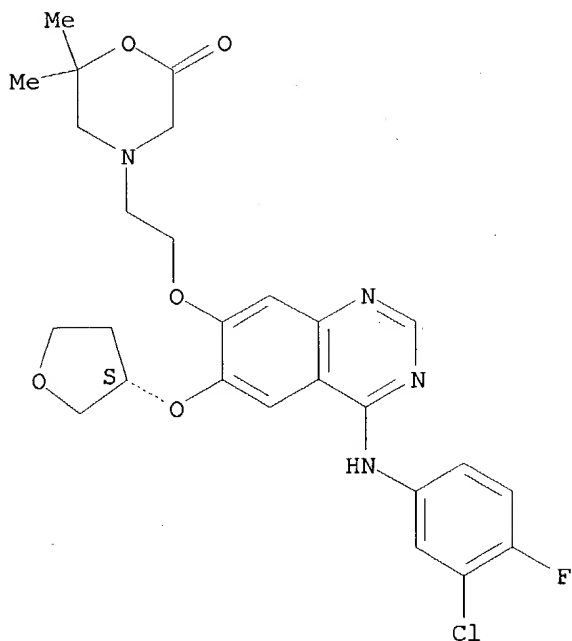


RN 402735-11-9 CAPLUS

CN 2-Morpholinone, 4-[2-[[4-[(3-chloro-4-fluorophenyl)amino]-6-[(3S)-tetrahydro-3-furanyl]oxy]-7-quinazolinyl]oxy]ethyl]-6,6-dimethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

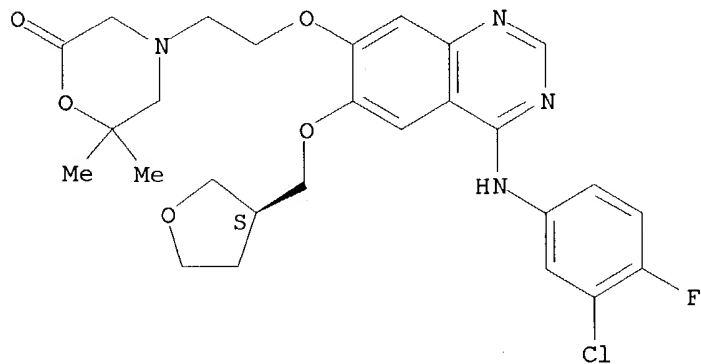
09/938,235



RN 402735-13-1 CAPLUS

CN 2-Morpholinone, 4-[2-[[4-[(3-chloro-4-fluorophenyl)amino]-6-[[[(3S)-tetrahydro-3-furanyl]methoxy]-7-quinazolinyl]oxy]ethyl]-6,6-dimethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 10 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2001:762992 CAPLUS

DOCUMENT NUMBER: 135:303907

TITLE: Preparation of quinazolines as inhibitors of epidermal growth factor-mediated signal transduction.

INVENTOR(S): Himmelsbach, Frank; Langkopf, Elke; Jung, Birgit; Blech, Stefan; Solca, Flavio

PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma K.-G., Germany

SOURCE: PCT Int. Appl., 95 pp.

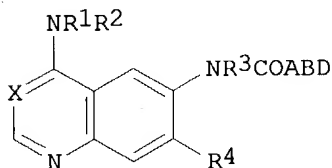
CODEN: PIXXD2

DOCUMENT TYPE: Patent

09/938,235

LANGUAGE: German
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001077104	A1	20011018	WO 2001-EP3694	20010331
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 10017539	A1	20011011	DE 2000-10017539	20000408
DE 10040525	A1	20020228	DE 2000-10040525	20000818
AU 2001063831	A5	20011023	AU 2001-63831	20010331
EP 1280798	A1	20030205	EP 2001-938076	20010331
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003530395	T2	20031014	JP 2001-575577	20010331
PRIORITY APPLN. INFO.: DE 2000-10017539 A 20000408 DE 2000-10040525 A 20000818 WO 2001-EP3694 W 20010331				
OTHER SOURCE(S): MARPAT 135:303907 GI				



AB Title compds. [I; X = NCN, N; R1 = H, alkyl; R2 = (substituted) Ph, PhCH2, PhCH2CH2; R3 = H, alkyl; R4 = H, alkoxy, cycloalkoxy, cycloalkylalkoxy; A = (substituted) vinylene; B = bond, (fluoro)alkylene; D = substituted pyrrolidinyl, piperidinyl, piperazinyl, etc.], were prepared Thus, 4-[(3-chloro-4-fluorophenyl)amino]-6-[[4-(piperazin-1-yl)-1-oxo-2-buten-1-yl]amino]-7-cyclopropylmethoxyquinazoline (preparation given) in THF was treated with Et3N and then with 3-bromodihydrofuran-2-one in THF under ice cooling followed by stirring for 48 h at room temperature to give 56% 4-[(3-chloro-4-fluorophenyl)amino]-6-[[4-[4-(2-oxotetrahydrofuran-3-yl)piperazin-1-yl]-1-oxo-2-buten-1-yl]amino]-7-cyclopropylmethoxyquinazoline. The latter inhibited epidermal growth factor (EGF)-dependent proliferation of F/L-HERc cells with IC50 = 0.05 nM.

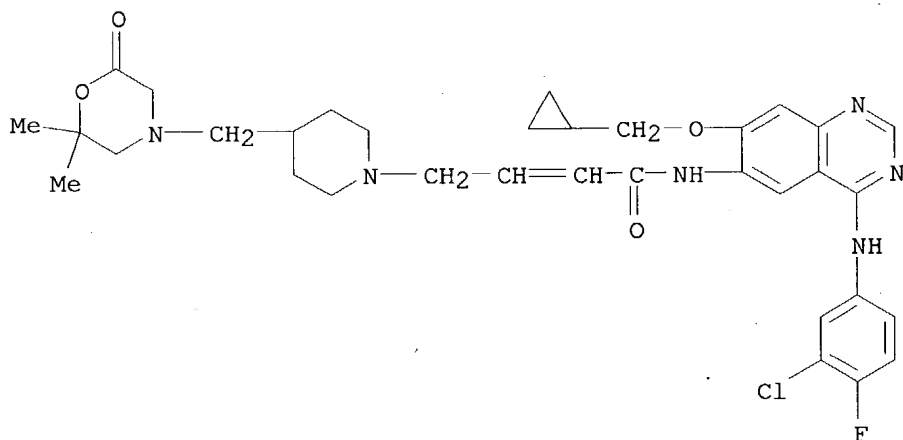
IT 365532-49-6P 367282-23-3P 367282-25-5P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation of quinazolines as inhibitors of epidermal growth factor-mediated signal transduction)

09/938,235

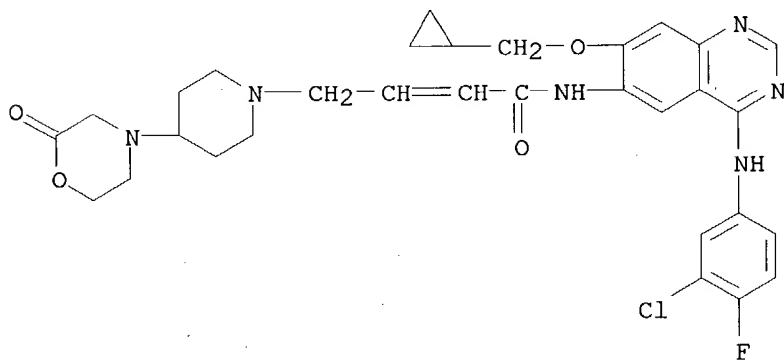
RN 365532-49-6 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[4-[(2,2-dimethyl-6-oxo-4-morpholinyl)methyl]-1-piperidinyl]- (9CI) (CA INDEX NAME)



RN 367282-23-3 CAPLUS

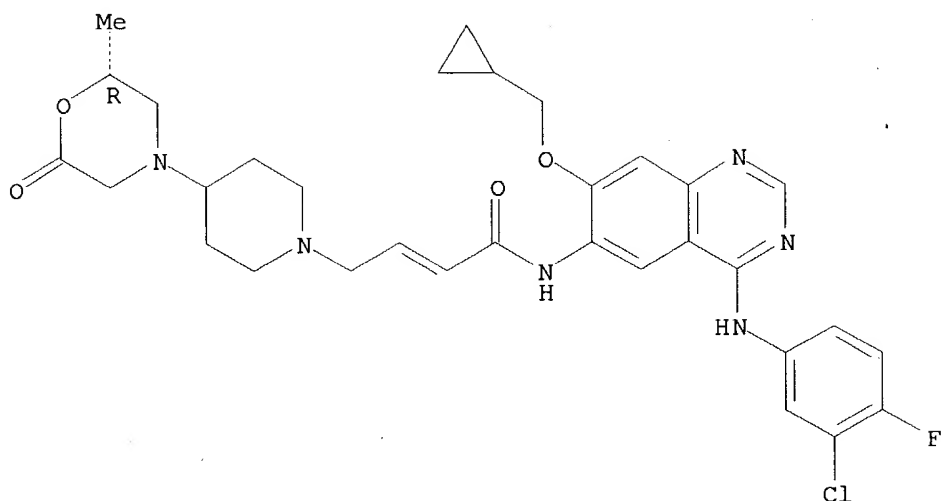
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[4-(2-oxo-4-morpholinyl)-1-piperidinyl]- (9CI) (CA INDEX NAME)



RN 367282-25-5 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[4-[(2R)-2-methyl-6-oxo-4-morpholinyl]-1-piperidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 11 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2001:747043 CAPLUS

DOCUMENT NUMBER: 135:303901

TITLE: Bicyclic heterocycles as inhibitors of epidermal growth factor receptor mediated signal transduction

INVENTOR(S): Himmelsbach, Frank; Langkopf, Elke; Jung, Birgit; Blech, Stefan; Solca, Flavio

PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma KG, Germany

SOURCE: Ger. Offen., 28 pp.

CODEN: GWXXBX

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 2

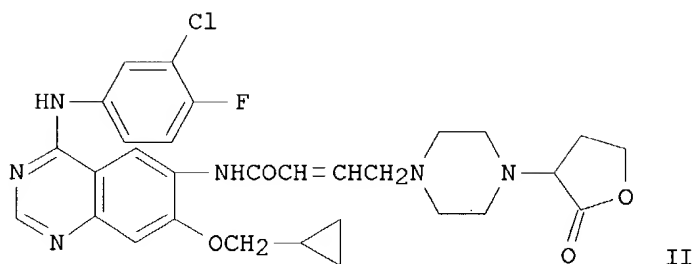
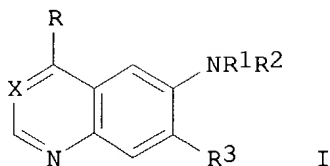
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10017539	A1	20011011	DE 2000-10017539	20000408
US 2001044435	A1	20011122	US 2001-816003	20010323
US 6627634	B2	20030930		
WO 2001077104	A1	20011018	WO 2001-EP3694	20010331
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2001063831	A5	20011023	AU 2001-63831	20010331
EP 1280798	A1	20030205	EP 2001-938076	20010331
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003530395	T2	20031014	JP 2001-575577	20010331
PRIORITY APPLN. INFO.:			DE 2000-10017539	A 20000408
			DE 2000-10040525	A 20000818

OTHER SOURCE(S):

MARPAT 135:303901

GI



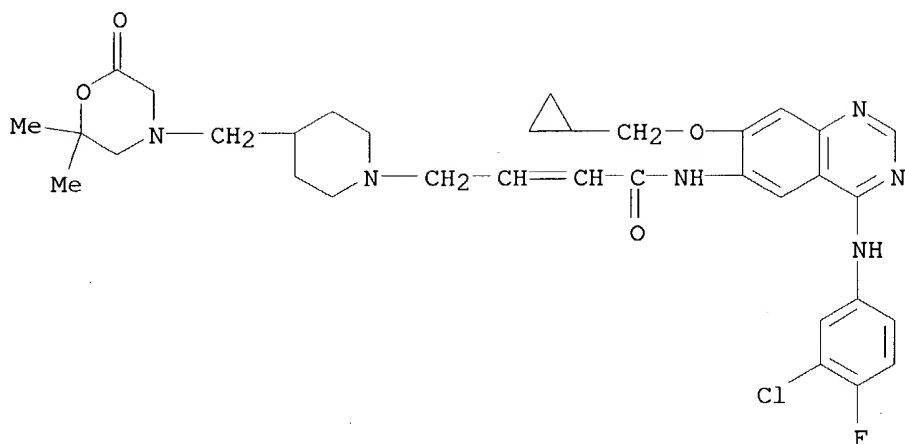
AB Bicyclic heterocycles I [X = N, CCN; R = substituted NH₂; R₁ = H, alkyl; R₂ = acyl; R₃ = H, (un)substituted alkoxy, cycloalkoxy, tetrahydrofuranyloxy, tetrahydropyranyloxy, tetrahydrofuranylmethoxy, tetrahydropyranylmethoxy] were prepared for use as inhibitors of tyrosine kinase-mediated signal transduction for treatment of tumors and diseases of the lung and airway. Thus, 4-[(3-chloro-4-fluorophenyl)amino]-7-fluoro-6-nitroquinazoline was treated with cyclopropylmethanol, followed by reduction to the amine, reaction with 4-bromocrotonic acid and N-tert.-butoxycarbonylpiperazine, and deblocking to give the quinazoline II. II had an IC₅₀ for inhibition of epidermal growth factor dependent proliferation of 0.05 nM.

IT **365532-49-6P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of bicyclic heterocycles as inhibitors of epidermal growth factor receptor mediated signal transduction)

RN 365532-49-6 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[4-[(2,2-dimethyl-6-oxo-4-morpholinyl)methyl]-1-piperidinyl]- (9CI) (CA INDEX NAME)



L3 ANSWER 12 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN
 ACCESSION NUMBER: 2000:666715 CAPLUS
 DOCUMENT NUMBER: 133:252449
 TITLE: Quinazolines and other bicyclic heterocycles,
 pharmaceutical compositions containing these compounds
 as tyrosine kinase inhibitors, and processes for
 preparing them
 INVENTOR(S): Himmelsbach, Frank; Langkopf, Elke; Blech, Stefan;
 Jung, Birgit; Metz, Thomas; Solca, Flavio
 PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma K.-G., Germany
 SOURCE: PCT Int. Appl., 153 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

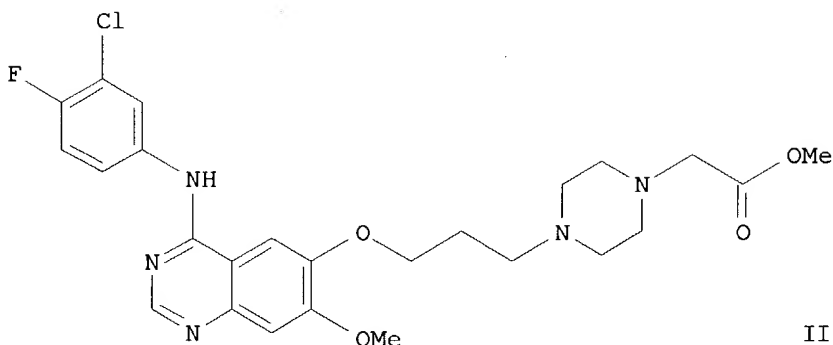
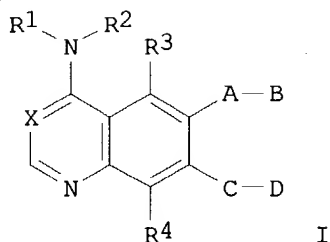
present app

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000055141	A1	20000921	WO 2000-EP2228	20000314
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 19911509	A1	20000921	DE 1999-19911509	19990315
EP 1163227	A1	20011219	EP 2000-909360	20000314
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 2000009076	A	20011226	BR 2000-9076	20000314
TR 200102782	T2	20020422	TR 2001-200102782	20000314
JP 2002539199	T2	20021119	JP 2000-605571	20000314
EE 200100484	A	20021216	EE 2001-484	20000314
NZ 514706	A	20031128	NZ 2000-514706	20000314
AU 772520	B2	20040429	AU 2000-31667	20000314
US 2002177601	A1	20021128	US 2001-938235	20010823
ZA 2001007185	A	20020621	ZA 2001-7185	20010830

09/938,235

BG 105893	A	20020531	BG 2001-105893	20010912
NO 2001004487	A	20010914	NO 2001-4487	20010914
PRIORITY APPLN. INFO.:			DE 1999-19911509	A 19990315
			WO 2000-EP2228	W 20000314

OTHER SOURCE(S): MARPAT 133:252449
GI



AB The invention relates to bicyclic heterocyclic compds. I [R1 = H, alkyl; R2 = (un)substituted Ph, CH2Ph, or CH(Me)Ph; R3, R4 = H, F, Cl, OMe, or Me optionally substituted by OMe, NMe2, NEt2, pyrrolidino, piperidino, or morpholino; X = N or C(CN); A = O, NH, (un)substituted alkylene, O-alkylene, NH-alkylene, O-cycloalkylene, etc.; B = (un)substituted amine-containing sidechain, piperazino, alkyleneimino, morpholino, etc.; or AB = H, F, Cl, alkoxy, amino, etc.; C = groups similar to A; D = groups similar to B; with a variety of provisos] and their tautomers, stereoisomers, and salts, and particularly their physiol. acceptable salts with inorg. or organic acids or bases. The compds. have valuable pharmacol. properties, particularly an inhibitory effect on signal transduction mediated by tyrosine kinases, and are useful in treating diseases, particularly tumor diseases, and diseases of the lung and airways. Over 20 compds. were prepared, and over 200 are listed. For instance, alkylation of 4-(3-chloro-4-fluorophenylamino)-6-[3-(1-piperazinyl)propyloxy]-7-methoxyquinazoline (preparation given) by Me bromoacetate gave 51% title compound

II. The latter compound inhibited EGF-dependent proliferation of F/L-HERC cells in vitro, with an IC50 of 46 nM.

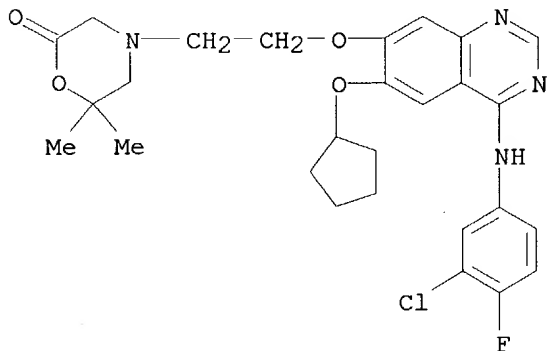
IT **295330-30-2P**, 4-[(3-Chloro-4-fluorophenyl)amino]-6-cyclopentyloxy-7-[2-(6,6-dimethyl-2-oxomorpholin-4-yl)ethoxy]quinazoline
295330-32-4P, 4-[(3-Bromophenyl)amino]-6-[2-(6,6-dimethyl-2-oxomorpholin-4-yl)ethoxy]-7-methoxyquinazoline

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug candidate; preparation of quinazoline derivs. and other bicyclic heterocycles as tyrosine kinase inhibitors)

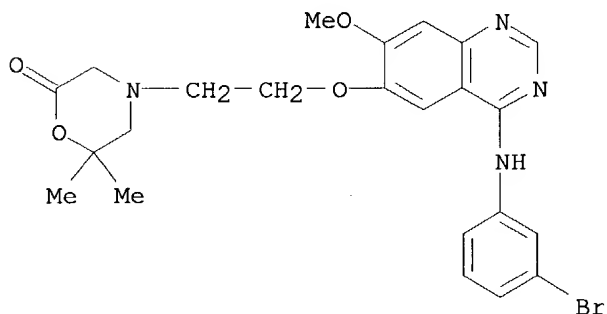
RN 295330-30-2 CAPLUS

CN 2-Morpholinone, 4-[2-[[4-[(3-chloro-4-fluorophenyl)amino]-6-(cyclopentyloxy)-7-quinazolinyl]oxy]ethyl]-6,6-dimethyl- (9CI) (CA INDEX NAME)



RN 295330-32-4 CAPLUS

CN 2-Morpholinone, 4-[2-[[4-[(3-bromophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]ethyl]-6,6-dimethyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 13 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2000:628125 CAPLUS

DOCUMENT NUMBER: 133:207919

TITLE: Preparation of 4-amino-quinazoline and quinoline derivatives having an inhibitory effect on signal transduction mediated by tyrosine kinases useful for treating tumoral diseases, lung and respiratory tract diseases

INVENTOR(S): Himmelsbach, Frank; Langkopf, Elke; Jung, Birgit; Metz, Thomas; Solca, Flavio; Blech, Stefan

PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma K.-G., Germany

SOURCE: PCT Int. Appl., 232 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

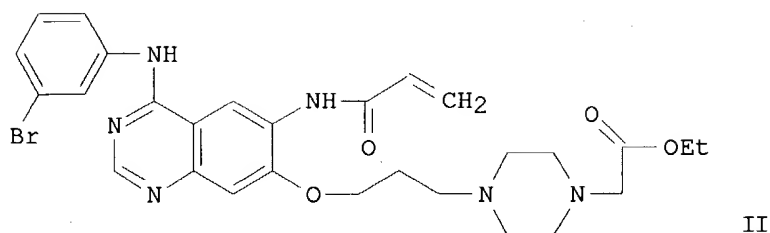
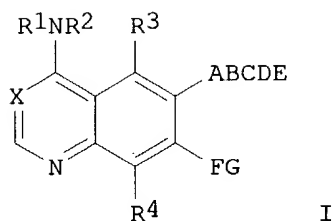
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

*assigned
only provisional*

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000051991	A1	20000908	WO 2000-EP1496	20000224
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 19908567	A1	20000831	DE 1999-19908567	19990227
DE 19911366	A1	20000921	DE 1999-19911366	19990315
DE 19928306	A1	20001228	DE 1999-19928306	19990621
DE 19954816	A1	20010517	DE 1999-19954816	19991113
CA 2361174	AA	20000908	CA 2000-2361174	20000224
EP 1157011	A1	20011128	EP 2000-910695	20000224
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 2000008524	A	20011218	BR 2000-8524	20000224
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BG 105765	A	20020329	BG 2001-105765	20010801
HR 2001000617	A1	20021031	HR 2001-617	20010823
NO 2001004114	A	20011015	NO 2001-4114	20010824
PRIORITY APPLN. INFO.:			DE 1999-19908567	A 19990227
			DE 1999-19911366	A 19990315
			DE 1999-19928306	A 19990621
			US 1999-149329P	P 19990817
			DE 1999-19954816	A 19991113
			WO 2000-EP1496	W 20000224
OTHER SOURCE(S):			MARPAT 133:207919	
GI				



AB Title compds. [I; R1 = H, C1-C4-alkyl; R2 = (un)substituted Ph, benzyl, 1-phenylethyl; R3, R4 independently = H, F, Cl, CH3O, CH3OCH2, (CH3)2NCH2, (CH3CH2)2NCH2, pyrrolidino, piperidino, morpholino; X = C(CN), N; A = O, NH, (C1-C4)-alkylN; B = CO, SO2; C = 1,3-allenylene, 1,1-vinylene, 1,2-vinylene, 1,3-butadien-1,4-ylene, with CH3, CF3 substitution; D = alkylene, CO-alkylene, SO2-alkylene; CO, SO2; E = HOCO(CH2)nNR5, (HO)2P(:O)(CH2)nNR5; n = 1-6; R5 = H, alkyl], tautomers, stereoisomers, and physiol. acceptable salts are prepared and having valuable pharmacol. properties, particularly an inhibiting effect on signal transduction mediated by tyrosine kinases. Title compds. are useful for treating tumoral diseases, diseases of the lungs and respiratory tract. Thus, the title compound II was prepared and tested by Cell Titer 96TM Aqueous Nonradioactive Cell Proliferation Assay.

IT **290302-25-9P**

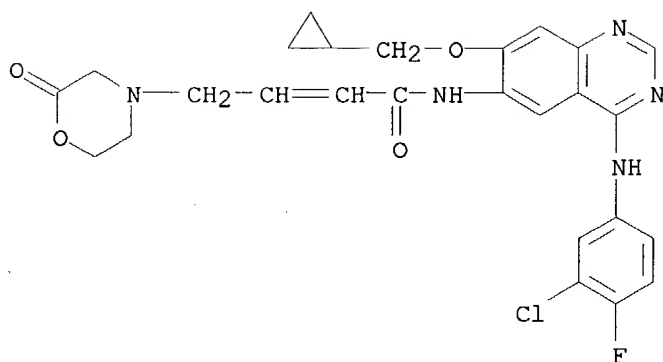
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of aminoquinazoline and aminoquinoline derivs. having an inhibitory effect on signal transduction mediated by tyrosine kinases useful for treating tumoral diseases, lung and respiratory tract diseases)

RN 290302-25-9 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(2-oxo-4-morpholinyl)- (9CI) (CA INDEX NAME)

09/938,235



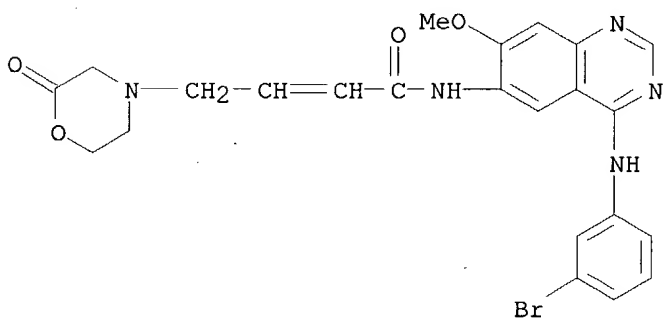
IT 290301-98-3P 290302-51-1P 290302-53-3P
290303-02-5P 290303-03-6P

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of aminoquinazoline and aminoquinoline derivs. having an inhibitory effect on signal transduction mediated by tyrosine kinases useful for treating tumoral diseases, lung and respiratory tract diseases)

RN 290301-98-3 CAPLUS

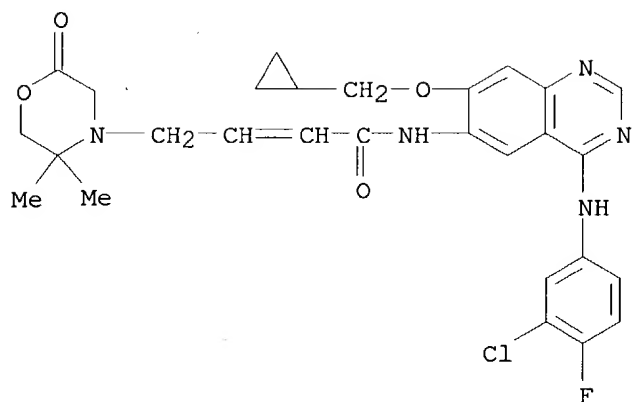
CN 2-Butenamide, N-[4-[(3-bromophenyl)amino]-7-methoxy-6-quinazolinyl]-4-(2-oxo-4-morpholinyl)- (9CI) (CA INDEX NAME)



RN 290302-51-1 CAPLUS

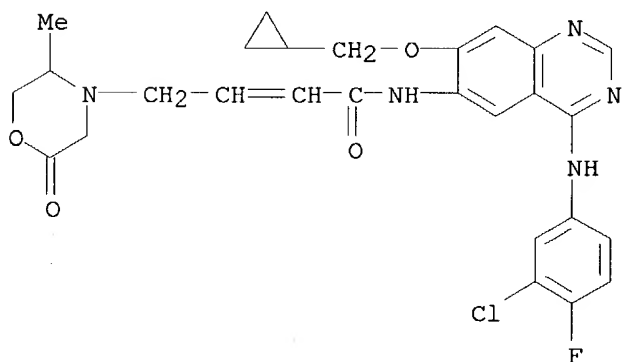
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(5,5-dimethyl-2-oxo-4-morpholinyl)- (9CI) (CA INDEX NAME)

09/938,235



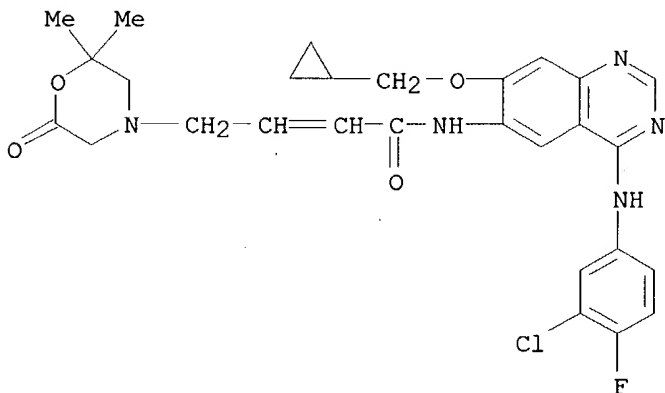
RN 290302-53-3 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(5-methyl-2-oxo-4-morpholinyl)- (9CI) (CA INDEX NAME)



RN 290303-02-5 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(2,2-dimethyl-6-oxo-4-morpholinyl)- (9CI) (CA INDEX NAME)



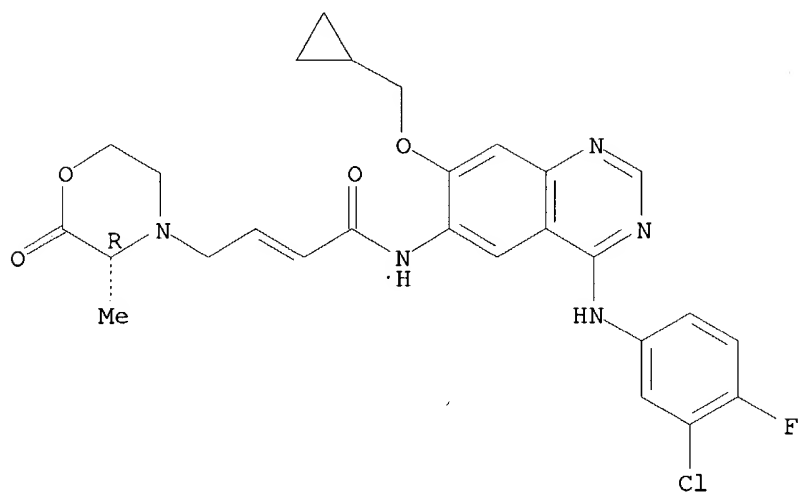
RN 290303-03-6 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-

09/938,235

6-quinazolinyl]-4-[(3R)-3-methyl-2-oxo-4-morpholinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



REFERENCE COUNT:

3

THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT